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#### (54) Title: CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES: USES THEREFOR

#### (57) Abstract

Novel chimeric nucleic acids, encoding chimeric *Borrelia* proteins consisting of at least two antigenic polypeptides from corresponding and/or non-corresponding proteins from the same and/or different species of *Borrelia*, are disclosed. Chimeric proteins encoded by the nucleic acid sequences are also disclosed. The chimeric proteins are useful as vaccine immunogens against Lyme borreliosis, as well as for immunodiagnostic reagents.

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## CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES; USES THEREFOR

#### Background of the Invention

Lyme borreliosis is the most common tick-borne infectious disease in North America, Europe, and northern Asia. The causative bacterial agent of this disease, Borrelia burgdorferi, was first isolated and cultivated in 1982 (Burgdorferi, W.A. et al., Science 216: 1317-1319 (1982); Steere, A.R. et al., N. Engl. J. 10 Med. 308: 733-740 (1983)). With that discovery, a wide array of clinical syndromes, described in both the European and American literature since the early 20th century, could be attributed to infection by B. burgdorferi (Afzelius, A., Acta Derm. Venereol. 2: 120-15 125 (1921); Bannwarth, A., Arch. Psychiatr. Nervenkrankh. 117: 161-185 (1944); Garin, C. and A. Bujadouz, J. Med. Lyon 71: 765-767 (1922); Herxheimer, K. and K. Hartmann, Arch. Dermatol. Syphilol. 61: 57-76, 255-300 (1902)).

- The immune response to B. burgdorferi is characterized by an early, prominent, and persistent humoral response to the end of lagellar protein, p41 (fla), and to a protein constituent of the protoplasmic cylinder, p93 (Szczepanski, A., and J.L. Benach,
- Microbiol. Rev. 55:21 (1991)). The p41 flagellin antigen is an immunodominant protein; however, it shares significant homology with flagellins of other microorganisms and therefore is highly cross reactive. The p93 antigen is the largest immunodominant antigen of
- 30 B. burgdorferi. Both the p41 and p93 proteins are physically cryptic antigens, sheathed from the immune system by an outer membrane whose major protein constituents are the outer surface proteins A and B

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(OspA and OspB). OspA is a basic lipoprotein of approximately 31 kd, which is encoded on a large linear plasmid along with OspB, a basic lipoprotein of approximately 34 kd (Szczepanski, A., and J.L. Benach, 5 Microbiol. Rev. 55:21 (1991)). Analysis of isolates of B. burgdorferi obtained from North America and Europe has demonstrated that OspA has antigenic variability, and that several distinct groups can be serologically and genotypically defined (Wilske, B., et al., World J. 10 Microbiol. 7: 130 (1991)). Other Borrelia proteins demonstrate similar antigenic variability. Surprisingly, the immune response to these outer surface proteins tends to occur late in the disease, if at all (Craft, J. E. et al., <u>J. Clin Invest. 78</u>: 934-939 15 (1986); Dattwyler, R.J. and B.J. Luft, Rheum. Clin. North Am. 15: 727-734 (1989)). Furthermore, patients acutely and chronically infected with B. burgdorferi respond variably to the different antigens, including OspA, OspB, OspC, OspD, p39, p41 and p93.

Vaccines against Lyme borreliosis have been 20 attempted. Mice immunized with a recombinant form of OspA are protected from challenge with the same strain of B. burgdorferi from which the protein was obtained (Fikrig, E., et al., Science 250: 553-556 (1990)). 25 Furthermore, passively transferred anti-OspA monoclonal antibodies (Mabs) have been shown to be protective in mice, and vaccination with a recombinant protein induced protective immunity against subsequent infection with the homologous strain of B.burgdorferi (Simon, M.M., et 30 al., J. Infect. Dis. 164: 123 (1991)). Unfortunately, immunization with a protein from one strain does not necessarily confer resistance to a heterologous strain (Fikrig, E. et al., <u>J. Immunol. 7</u>: 2256-1160 (1992)), but rather, is limited to the homologous 'species' from 35 which the protein was prepared. Furthermore,

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immunization with a single protein from a particular strain of Borrelia will not confer resistance to that strain in all individuals. There is considerable variation displayed in OspA and OspB, as well as p93, including the regions conferring antigenicity. Therefore, the degree and frequency of protection from vaccination with a protein from a single strain depend upon the response of the immune system to the particular variation, as well as the frequency of genetic variation in B. burgdorferi. Currently, a need exists for a vaccine which provides immunogenicity across species and to more epitopes within a species, as well as immunogenicity against more than one protein.

#### Summary of the Invention

The current invention pertains to chimeric Borrelia 15 proteins which include two or more antigenic Borrelia polypeptides which do not occur naturally (in nature) in the same protein in Borrelia, as well as the nucleic acids encoding such chimeric proteins. The antigenic 20 polypeptides incorporated in the chimeric proteins are derived from any Borrelia protein from any strain of Borrelia, and include outer surface protein (Osp) A, OspB, OspC, OspD, p12, p39, p41, p66, and p93. The proteins from which the antigenic polypeptides are 25 derived can be from the same strain of Borrelia, from different strains, or from combinations of proteins from the same and from different strains. If the proteins from which the antigenic polypeptides are derived are OspA or OspB, the antigenic polypeptides can be derived 30 from either the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein (referred to as a proximal portion), or the portion of the OspA or OspB protein present between the conserved tryptophan of the protein

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and the carboxy terminus (referred to as a distal portion). Particular chimeric proteins, and the nucleotide sequences encoding them, are set forth in Figures 23-37 and 43-46.

The chimeric proteins of the current invention provide antigenic polypeptides of a variety of Borrelia strains and/or proteins within a single protein. proteins are particularly useful in immunodiagostic assays to detect the presence of antibodies to native 10 Borrelia in potentially infected individuals as well as to measure T-cell reactivity, and can therefore be used as immunodiagnostic reagents. The chimeric proteins of the current invention are additionally useful as vaccine immunogens against Borrelia infection.

For a better understanding of the present invention 15 together with other and further objects, reference is made to the following description, taken together with the accompanying drawings.

#### Brief Description of the Drawings

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Figure 1 summarizes peptides and antigenic domains localized by proteolytic and chemical fragmentation of OspA.

Figure 2 is a comparison of the antigenic domains depicted in Figure 1, for OspA in nine strains of B. 25 burgdorferi.

Figure 3 is a graph depicting a plot of weighted polymorphism versus amino acid position among 14 OspA variants. The marked peaks are: a) amino acids 132-145; b) amino acids 163-177; c) amino acids 208-221. 30 lower dotted line at polymorphism value 1.395 demarcates statistically significant excesses of polymorphism at p The upper dotted line at 1.520 is the same, except that the first 29 amino acids at the monomorphic N-terminus have been removed from the original analysis.

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Figure 4 depicts the amino acid alignment of residues 200 through 220 for OspAs from strains B31 and K48 as well as for the site-directed mutants 613, 625, 640, 613/625, and 613/640. Arrow indicates Trp216.

5 Amino acid changes are underlined.

Figure 5 is a helical wheel projection of residues 204-217 of B31 OspA. Capital letters indicate hydrophobic residues; lower case letters indicate hydrophilic residues; +/- indicate positively/negatively charged residues. Dashed line indicates division of the alpha-helix into hydrophobic arc (above the line) and polar arc (below the line). Adapted from France et al. (Biochem. Biophys. Acta 1120: 59 (1992)).

Figure 6 depicts a phylogenic tree for strains of

Borrelia described in Table I. The strains are as

follows: 1 = B31; 2 = Pka1; 3 = ZS7; 4 = N40; 5 =

25015; 6 = K48; 7 = DK29; 8 = PHei; 9 = Ip90; 10 =

PTrob; 11 = ACAI; 12 = PGau; 13 = Ip3; 14 = PBo; 15 =

PKo.

Figure 7 depicts the nucleic acid sequence of OspA-B31 (SEW ID NO. 6), and the encoded protein sequence (SEQ ID NO. 7).

Figure 8 depicts the nucleic acid sequence of OspA-K48 (SEQ ID NO. 8), and the encoded protein sequence 25 (SEQ ID NO. 9).

Figure 9 depicts the nucleic acid sequence of OspA-PGau (SEQ ID NO. 10), and the encoded protein sequence (SEQ ID NO. 11).

Figure 10 depicts the nucleic acid sequence of 30 OspA-25015 (SEQ ID NO. 12), and the encoded protein sequence (SEQ ID NO. 13).

Figure 11 depicts the nucleic acid sequence of OspB-B31 (SEQ ID NO. 21), and the encoded protein sequence (SEQ ID NO. 22).

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Figure 12 depicts the nucleic acid sequence of OspC-B31 (SEQ ID NO. 29), and the encoded protein sequence (SEQ ID NO. 30).

Figure 13 depicts the nucleic acid sequence of 0spC-K48 (SEQ ID NO. 31), and the encoded protein sequence (SEQ ID NO. 32).

Figure 14 depicts the nucleic acid sequence of OspC-PKo (SEQ ID NO. 33), and the encoded protein sequence (SEQ ID NO. 34).

10 Figure 15 depicts the nucleic acid sequence of OspC-pTrob (SEQ ID NO. 35) and the encoded protein sequence (SEQ ID NO. 36).

Figure 16 depicts the nucleic acid sequence of p93-B31 (SEQ ID NO. 65) and the encoded protein sequence (SEQ ID NO. 66).

Figure 17 depicts the nucleic acid sequence of p93-K48 (SEQ ID NO. 67).

Figure 18 depicts the nucleic acid sequence of p93-PBo (SEQ ID NO. 69).

Figure 19 depicts the nucleic acid sequence of p93-pTrob (SEQ ID NO. 71).

Figure 20 depicts the nucleic acid sequence of p93-pGau (SEQ ID NO. 73).

Figure 21 depicts the nucleic acid sequence of p93-25 25015 (SEQ ID NO. 75).

Figure 22 depicts the nucleic acid sequence of p93-pKo (SEQ ID NO. 77).

Figure 23 depicts the nucleic acid sequence of the OspA-K48/OspA-PGau chimer (SEQ ID NO. 85) and the encoded chimeric protein sequence (SEQ ID NO. 86).

Figure 24 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau chimer (SEQ ID NO. 88) and the encoded chimeric protein sequence (SEQ ID NO. 89).

Figure 25 depicts the nucleic acid sequence of the OspA-B31/OspA-K48 chimer (SEQ ID NO. 91) and the encoded chimeric protein sequence (SEQ ID NO. 92).

Figure 26 depicts the nucleic acid sequence of the 5 OspA-B31/OspA-25015 chimer (SEQ ID NO. 94) and the encoded chimeric protein sequence (SEQ ID NO. 95).

Figure 27 depicts the nucleic acid sequence of the OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 97) and the encoded chimeric protein sequence (SEQ ID NO. 98).

Figure 28 depicts the nucleic acid sequence of the OspA-B31/OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 100) and the encoded chimeric protein sequence (SEQ ID NO. 101).

Figure 29 depicts the nucleic acid sequence of the 15 OspA-B31/OspB-B31 chimer (SEQ ID NO. 103) and the encoded chimeric protein sequence (SEQ ID NO. 104).

Figure 30 depicts the nucleic acid sequence of the OspA-B31/OspB-B31/OspC-B31 chimer (SEQ ID NO. 106) and the encoded chimeric protein sequence (SEQ ID NO. 107).

Figure 31 depicts the nucleic acid sequence of the OspC-B31/OspA-B31/OspB-B31 chimer (SEQ ID NO. 109) and the encoded chimeric protein sequence (SEQ ID NO. 110).

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Figure 32 depicts the nucleic acid sequence of the OspA-B31/p93-B31 chimer (SEQ ID NO. 111) and the encoded chimeric protein sequence (SEQ ID NO. 112).

Figure 33 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-234) chimer (SEQ ID NO. 113) and the encoded chimeric protein sequence (SEQ ID NO. 114).

Figure 34 depicts the nucleic acid sequence of the 30 OspB-B31/p41-B31 (122-295) chimer (SEQ ID NO. 115) and the encoded chimeric protein sequence (SEQ ID NO. 116).

Figure 35 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-234) chimer (SEQ ID NO. 117) and the encoded chimeric protein sequence (SEQ ID NO. 118).

Figure 36 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-295) chimer (SEQ ID NO. 119) and the encoded chimeric protein sequence (SEQ ID NO. 120).

Figure 37 depicts the nucleic acid sequence of the 5 OspB-B31/p41-B31 (122-234)/OspC-B31 chimer (SEQ ID NO. 121) and the encoded chimeric protein sequence (SEQ ID NO. 122).

Figure 38 depicts an alignment of the nucleic acid sequences for OspC-B31 (SEQ ID NO. 29), OspC-PKo (SEQ ID NO. 33), OspC-pTrob (SEQ ID NO. 35), and OspC-K48 (SEQ ID NO. 31). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspC-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 39 depicts an alignment of the nucleic acid sequences for OspD-pBO (SEQ ID NO. 123), OspD-PGau (SEQ ID NO. 124), OspD-DK29 (SEQ ID NO. 125), and OspD-K48 (SEQ ID NO. 126). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspD-pBo) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 40 depicts the nucleic acid sequence of p41-B31 (SEq ID NO. 127) and then encoded protein sequence (SEQ ID NO. 128).

Figure 41 depicts an alignment of the nucleic acid sequences for p41-B31 (SEQ ID NO. 127), p41-pKa1 (SEQ ID NO. 129), p41-pGau (SEQ ID NO. 51), p41-pBo (SEQ ID NO. 130), p41-DK29 (SEQ ID NO. 53), and p41-pKo (SEQ ID NO. 131). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, p41-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 42 depicts an alignment of the nucleic acid sequences for OspA-B31 (SEQ ID NO. 6), OspA-pKa1 (SEQ ID NO. 132), OspA-N40 (SEQ ID NO. 133), OspA-ZS7 (SEQ ID

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NO. 134), OspA-25015 (SEQ ID NO. 12), OspA-pTrob (SEQ ID NO. 135), OspA-K48 (SEQ ID NO. 8), OspA-Hei (SEQ ID NO. 136), OspA-DK29 (SEQ ID NO. 49), OSpA-Ip90 (SEQ ID NO. 50), OspA-pBo (Seq ID NO. 55), OspA-Ip3 (SEQ ID NO. 56), OspA-PKo (SEQ ID NO. 57), OspA-ACAI (SEQ ID NO. 58), and OspA-PGau (SEQ ID NO. 10). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspA-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 43 depicts the nucleic acid sequence of the OspA-Tro/OspA-Bo chimer (SEQ ID NO. 137) and the encoded chimeric protein sequence (SEQ ID NO. 138).

Figure 44 depicts the nucleic acid sequence of the OspA-PGau/OspA-Bo chimer (SEQ ID NO. 139) and the encoded chimeric protein sequence (SEQ ID NO. 140).

Figure 45 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 141) and the encoded chimeric protein sequence (SEQ ID NO. 142).

Figure 46 depicts the nucleic acid sequence of the OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 143) and the encoded chimeric protein sequence (SEQ ID NO. 144).

#### Detailed Description of the Invention

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The current invention pertains to chimeric proteins
comprising antigenic Borrelia polypeptides which do not
occur in nature in the same Borrelia protein. The
chimeric proteins are a combination of two or more
antigenic polypeptides derived from Borrelia proteins.
The antigenic polypeptides can be derived from different
proteins from the same species of Borrelia, or different
proteins from different Borrelia species, as well as
from corresponding proteins from different species. As
used herein, the term "chimeric protein" describes a
protein comprising two or more polypeptides which are

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derived from corresponding and/or non-corresponding native Borrelia protein. A polypeptide "derived from" a native Borrelia protein is a polypeptide which has an amino acid sequence the same as an amino acid sequence 5 present in a Borrelia protein, an amino acid sequence equivalent to the amino acid sequence of a naturally occurring Borrelia protein, or an amino acid sequence substantially similar to the amino acid sequence of a naturally occurring Borrelia protein (e.g., differing by 10 few amino acids) such as when a nucleic acid encoding a protein is subjected to site-directed mutagenesis. "Corresponding" proteins are equivalent proteins from different species or strains of Borrelia, such as outer surface protein A (OspA) from strain B31 and OspA from 15 strain K48. The invention additionally pertains to nucleic acids encoding these chimeric proteins.

As described below, Applicants have identified two separate antigenic domains of OspA and OspB which flank the sole conserved tryptophan present in OspA and in 20 OspB. These domains share cross-reactivity with different genospecies of Borrelia. The precise amino acids responsible for antigenic variability were determined through site-directed mutagenesis, so that proteins with specific amino acid substitutions are 25 available for the development of chimeric proteins. Furthermore, Applicants have identified immunologically important hypervariable domains in OspA proteins, as described below in Example 2. The first hypervariable domain of interest for chimeric proteins, Domain A, includes amino acid residues 120-140 of OspA, the second hypervariable domain, Domain B, includes residues 150-180 and the third hypervariable domain, Domain C, includes residues 200-216 or 217 (depending on the position of the sole conserved tryptophan residue in the 35 OspA of that particular species of Borrelia) (see Figure

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3). In addition, Applicants have sequenced the genes for several Borrelia proteins.

These discoveries have aided in the development of novel recombinant Borrelia proteins which include two or more amino acid regions or sequences which do not occur in the same Borrelia protein in nature. The recombinant proteins comprise polypeptides from a variety of Borrelia proteins, including, but not limited to, OspA, OspB, OspC, OspD, p12, p39, p41, p66, and p93.

On Antigenically relevant polypeptides from each of a

10 Antigenically relevant polypeptides from each of a number of proteins are combined into a single chimeric protein.

In one embodiment of the current invention, chimers are now available which include antigenic polypeptides 15 flanking a tryptophan residue. The antigenic polypeptides are derived from either the proximal portion from the tryptophan (the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein), or the distal 20 portion from the tryptophan (the portion of the OspA or OspB protein present between the conserved tryptophan of the protein and the carboxy terminus) in OspA and/or The resultant chimers can be OspA-OspA chimers (i.e., chimers incorporating polypeptides derived from 25 OspA from different strains of Borrelia), OspA-OspB chimers, or OspB-OspB chimers, and are constructed such that amino acid residues amino-proximal to an invariant tryptophan are from one protein and residues carboxyproximal to the invariant tryptophan are from the other 30 protein. For example, one available chimer consists of a polypeptide derived from the amino-proximal region of OspA from strain B31, followed by the tryptophan residue, followed by a polypeptide derived from the carboxy-proximal region of OspA from strain K48 (SEQ ID 35 NO. 92). Another available chimer includes a

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polypeptide derived from the amino-proximal region of OspA from strain B31, and a polypeptide derived from the carboxy-proximal region of OspB from strain B31 (SEQ ID NO. 104). If the polypeptide proximal to the tryptophan of these chimeric proteins is derived from OspA, the proximal polypeptide can be further subdivided into the three hypervariable domains (Domains A, B, and C), each of which can be derived from OspA from a different strain of Borrelia. These chimeric proteins can further comprise antigenic polypeptides from another protein, in addition to the antigenic polypeptides flanking the tryptophan residue.

In another embodiment of the current invention, chimeric proteins are available which incorporate

15 antigenic domains of two or more Borrelia proteins, such as Osp proteins (Osp A, B, C and/or D) as well as pl2, p39, p41, p66, and/or p93.

The chimers described herein can be produced so that they are highly soluble, hyper-produced in E. coli, and non-lipidated. In addition, the chimeric proteins can be designed to end in an affinity tag (His-tag) to facilitate purification. The recombinant proteins described herein have been constructed to maintain high levels of antigenicity. In addition, recombinant proteins specific for the various genospecies of Borrelia that cause Lyme disease are now available, because the genes from each of the major genospecies have been sequenced; the sequences are set forth below. These recombinant proteins with their novel biophysical and antigenic properties will be important diagnostic reagent and vaccine candidates.

The chimeric proteins of the current invention are advantageous in that they retain specific reactivity to monoclonal and polyclonal antibodies against wild-type Borrelia proteins, are immunogenic, and inhibit the

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growth or induce lysis of Borrelia in vitro.

Furthermore, in some embodiments, the proteins provide antigenic domains of two or more Borrelia strains and/or proteins within a single protein. Such proteins are particularly useful in immuno-diagostic assays. For example, proteins of the present invention can be used as reagents in assays to detect the presence of antibodies to native Borrelia in potentially infected individuals. These proteins can also be used as immunodiagnostic reagents, such as in dot blots, Western blots, enzyme linked immunosorbed assays, or agglutination assays. The chimeric proteins of the present invention can be produced by known techniques, such as by recombinant methodology, polymerase chain reaction, or mutagenesis.

Furthermore, the proteins of the current invention are useful as vaccine immunogens against Borrelia infection. Because Borrelia has been shown to be clonal, a protein comprising antigenic polypeptides from 20 a variety of Borrelia proteins and/or species, will provide immunoprotection for a considerable time when used in a vaccine. The lack of significant intragenic recombination, a process which might rapidly generate novel epitopes with changed antigenic properties, ensures that Borrelia can only change antigenic type by accumulating mutational change, which is slow when compared with recombination in generating different antigenic types. The chimeric protein can be combined with a physiologically acceptable carrier and administered to a vertebrate animal through standard methods (e.g., intravenously or intramuscularly, for example).

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The current invention is illustrated by the following Examples, which are not to be construed to be limiting in any way.

# Example 1. <u>Purification of Borrelia burgorferi Outer</u> 5 <u>Surface Protein A and Analysis of</u> Antibody Binding Domains

This example details a method for the purification of large amounts of native outer surface protein A (OspA) to homogeneity, and describes mapping of the antigenic specificities of several anti-OspA MAbs. OspA was purified to homogeneity by exploiting its resistance to trypsin digestion. Intrinsic labeling with <sup>14</sup>C-palmitic acid confirmed that OspA was lipidated, and partial digestion established lipidation at the aminoterminal cysteine of the molecule.

The reactivity of seven anti-OspA murine monoclonal antibodies to nine different Borrelia isolates was ascertained by Western blot analysis. Purified OspA was fragmented by enzymatic or chemical cleavage, and the monoclonal antibodies were able to define four distinct immunogenic domains (see Figure 1). Domain 3, which included residues 190-220 of OspA, was reactive with protective antibodies known to agglutinate the organism in vitro, and included distinct specificities, some of which were not restricted to a genotype of B. burgdorferi.

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#### Purification of Native OspA

Detergent solubilization of B. burgdorferi strips the outer surface proteins and yields partially-purified preparations containing both OspA and outer surface 5 protein B (Osp B) (Barbour, A.G. et al., Infect. Immun. 52 (5): 549-554 (1986); Coleman, J.L. and J.L. Benach, J Infect. Dis. 155 (4): 756-765 (1987); Cunningham, T.M. et al., Ann. NY Acad. Sci. 539: 376-378 (1988); Brandt, M.E. et al., <u>Infect. Immun. 58</u>: 983-991 (1990); Sambri, 10 V. and R. Cevenini, Microbiol. 14:307-314 (1991)). Although both OspA and OspB are sensitive to proteinase K digestion, in contrast to OspB, OspA is resistant to cleavage by trypsin (Dunn, J. et al., Prot. Exp. Purif. 1: 159-168 (1990); Barbour, A.G. et al., Infect. Immun. 15 45:94-100 (1984)). The relative insensitivity to trypsin is surprising in view of the fact that Osp A has a high (16% for B31) lysine content, and may relate to the relative configuration of Osp A and B in the outer membrane.

Intrinsic Radiolabeling of Borrelia Labeling for lipoproteins was performed as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). 14C-palmitic acid (ICN, Irvine, California) was added to the BSK II media to a final concentration of 25 0.5  $\mu$ Ci per milliliter (ml). Organisms were cultured at 34°C in this medium until a density of 108 cells per ml was achieved.

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Purification of OspA Protein from Borrelia Strain B31 Borrelia burgdorferi, either 14C-palmitic acid-30 labeled or unlabeled, were harvested and washed as described (Brandt, M.E. et al., Infect. Immun. 58:983-991 (1990)). Whole organisms were trypsinized according

to the protocol of Barbour et al. (Infect. Immun. 45:94-100 (1984)) with some modifications. The pellet was suspended in phosphate buffered saline (PBS, 10mM, pH 7.2), containing 0.8% tosyl-L-phenylalanine chloromethyl 5 ketone (TPCK)-treated trypsin (Sigma, St. Louis, Missouri), the latter at a ratio of 1  $\mu$ g per 10 $^{8}$  cells. Reaction was carried out at 25°C for 1 hour, following which the cells were centrifuged. The pellet was washed in PBS with 100  $\mu g/ml$  phenylmethylsulfonyl fluoride 10 (PMSF). Triton X-114 partitioning of the pellet was carried out as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). Following trypsin treatment, cells were resuspended in ice-cold 2% (V/V) Triton X-114 in PBS at 109 cells per ml. The suspension was rotated 15 overnight at 4°C, and the insoluble fraction removed as a pellet after centrifugation at 10,000 X g for 15 minutes at 4°C. The supernatant (soluble fraction) was incubated at 37°C for 15 minutes and centrifuged at room temperature at 1000 X g for 15 minutes to separate the 20 aqueous and detergent phases. The aqueous phase was decanted, and ice cold PBS added to the lower Triton phase, mixed, warmed to 37°C, and again centrifuged at 1000 X g for 15 minutes. Washing was repeated twice more. Finally, detergent was removed from the 25 preparation using a spin column of Bio-beads SM2 (BioRad, Melville, New York) as described (Holloway, P.W., Anal. Biochem. 53:304-308 (1973)).

Ion exchange chromatography was carried out as described by Dunn et al. (Prot. Exp. Purif. 1: 159-168 (1990)) with minor modifications. Crude OspA was dissolved in buffer A (1% Triton X-100, 10mM phosphate buffer (pH 5.0)) and loaded onto a SP Sepharose resin (Pharmacia, Piscataway, New Jersey), pre-equilibrated with buffer A at 25°C. After washing the column with 10

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bed-volumes of buffer A, the bound OspA was eluted with buffer B (1% Triton X-100, 10mM phosphate buffer (pH 8.0)). OspA fractions were detected by protein assay using the BCA method (Pierce, Rockford, Illinois), or as radioactivity when intrinsically labeled material was fractionated. Triton X-100 was removed using a spin column of Bio-beads SM2.

This method purifies OspA from an outer surface membrane preparation. In the absence of trypsin
treatment, OspA and B were the major components of the soluble fraction obtained after Triton partitioning of strain B31. In contrast, when Triton extraction was carried out after trypsin-treatment, the OspB band is not seen. Further purification of OspA-B31 on a SP

Sepharose column resulted in a single band by SDS-PAGE. The yield following removal of detergent was approximately 2 mg per liter of culture. This method of purification of OspA, as described herein for strain B31, can be used for other isolates of Borrelia as well.

For strains such as strain K48, which lack OspB, trypsin treatment can be omitted.

#### Lipidation site of OspA-B31

purified as described above and partially digested with endoproteinase Asp-N (data not shown). Following digestion, a new band of lower molecular weight was apparent by SDS-PAGE, found by direct amino-terminal sequencing to begin at Asp<sub>25</sub>. This band had no trace of radioactivity by autoradiography (data not shown). OspA and B contain a signal sequence (L-X-Y-C) similar to the consensus described for lipoproteins of E. coli, and it has been predicted that the lipidation site of OspA and B should be the amino-terminal cysteine (Brandt, M.E. et

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al., <u>Infect. Immun 58</u>: 983-991 (1990)). The results presented herein support this prediction.

### B. Comparison of OspA Antibody Binding Regions in Nine Strains of Borrelia burgdorferi

The availability of the amino acid sequenced for OspA from a number of different isolates, combined with peptide mapping and Western blot analysis, permitted the identification of the antigenic domains recognized by monoclonal antibodies (MAbs) and allowed inference of the key amino acid residues responsible for specific antibody reactivity.

Strains of Borrelia burgdorferi

Nine strains of *Borrelia*, including seven European strains and two North American strains, were used in this study of antibody binding domains of several proteins. Information concerning the strains is summarized in Table I, below.

Table I. Representative Borrelia Strains

Table I. Representative Boiletta Strains				
Strain	Location and Source	Reference for Strain		
K48	Czechoslovakia, Ixodes ricinus	none		
PGau	Germany, human ACA	Wilske, B. et al., <u>J. Clin.</u> <u>Microbiol. 32</u> :340-350 (1993)		
DK29	Denmark, human EM	Wilske, B. et al.		
PKo	Germany, human EM	Wilske, B. et al.		
PTrob	Germany, human skin	Wilske, B. et al.		
Ip3	Khabarovsk, Russia, I. persulcatus	Asbrink, E. et al., <u>Acta</u> <u>Derm. Venereol. 64</u> : 506-512 (1984)		
Ip90	Khabarovsk, Russia, I. persulcatus	Asbrink, E. et al.		
25015	Millbrook, NY, I. persulcatus	Barbour, A.G. et al., <u>Curr.</u> <u>Microbiol.</u> 8:123-126 (1983)		
B31	Shelter Island, NY, I. scapularis	Luft, B.J. et al., <u>Infect.</u> <u>Immun. 60</u> : 4309-4321 (1992); ATCC 35210		
PKa1	Germany, human CSF	Wilske, B. et al.		
ZS7	Freiburg, Germany, I. ricinus	Wallich, R. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 8864 (1989)		
N40	Westchester Co., NY	Fikrig, E. et al., <u>Science</u> 250:553-556 (1990)		
PHei	Germany, human CSF	Wilske, B. et al.		
ACAI	Sweden, human ACA	Luft, B. J. et al., <u>FEMS</u> <u>Microbiol. Lett. 93</u> :73-68 (1992)		
РВо	Germany, human CSF	Wilske, B. et al.		

ACA = patient with acrodermatitis chronica atrophicans; EM = patient with erythema migrans; CSF = cerebrospinal fluid of patient with Lyme disease

Strains K48, PGau and DK29 were supplied by R. Johnson, University of Minnesota; PKo and pTrob were provided by B. Wilske and V. Preac-Mursic of the

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Pettenkhofer Institute, Munich, Germany; and Ip3 and Ip90 were supplied by L. Mayer of the Center for Disease Control, Atlanta, Georgia. The North American strains included strain 25015, provided by J. Anderson of the Connecticut Department of Agriculture; and strain B31 (ATCC 35210).

#### Monoclonal Antibodies

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Seven monoclonal antibodies (MAbs) were utilized in this study. Five of the MAbs (12, 13, 15, 83 and 336) were 10 produced from hybridomas cloned and subcloned as previously described (Schubach, W.H., et al., Infect. Immun. 59(6):1911-1915 (1991)). MAb H5332 (Barbour, A.G. et al., Infect. Immun. 41:795-804 (1983)) was a gift from Drs. Alan Barbour, University of Texas, and MAb CIII.78 (Sears, J.E. 15 et al., <u>J. Immunol. 147</u>(6):1995-2000 (1991)) was a gift from Richard A. Flavell, Yale University. MAbs 12 and 15 were raised against whole sonicated B3; MAb 336 was produced against whole PGau; and MAbs 13 and 83 were raised to a truncated form of OspA cloned from the K48 strain and 20 expressed in E. coli using the T7 RNA polymerase system (McGrath, B.C. et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York, pp. 365-370 (1993)). All MAbs were typed as being Immunoglobulin G (IgG).

Methods of Protein Cleavage, Western Blotting, and Amino-Terminal Sequencing

Prediction of the various cleavage sites was achieved by knowledge of the primary amino acid sequence derived from the full nucleotide sequences of OspA, many of which are currently available (see Table II, below). Cleavage sites can also be predicted based on the peptide sequence of OspA, which can be determined by standard techniques after isolation and purification of OspA by the method described above. Cleavage of several OspA isolates was

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conducted to determine the localization of monoclonal antibody binding of the proteins.

Hydroxylamine-HCl (HA), N-chlorosuccinimide (NCS), and cyanogen bromide cleavage of OspA followed the methods 5 described by Bornstein (Biochem. 9 (12):2408-2421 (1970)), Shechter et al., (Biochem. 15 (23):5071-5075 (1976)), and Gross (in Hirs, C.H.W. (ed): Methods in Enzymology, (N.Y. Acad. Press), <u>11</u>:238-255 (1967)) respectively. Protease cleavage by endoproteinase, Asp-N (Boehringer Mannheim, 10 Indianapolis, Indiana), was performed as described by Cleveland D.W. et al., (J. Biol. Chem. 252:1102-1106 (1977)). Ten micrograms of OspA were used for each reaction. The ratio of enzyme to OspA was approximately 1 to 10 (w/w).

Proteins and peptides generated by cleavage were 15 separated by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) (Laemmli, U.K., <u>Nature</u> (London) <u>227</u>:680-685 (1970)), and electroblotted onto immobilon Polyvinylidine Difluoride (PVDF) membranes (Ploskal, M.G. et al., Biotechniques 20  $\underline{4}$ :272-283 (1986)). They were detected by amido black staining or by immunostaining with murine MAbs, followed by alkaline phosphatase-conjugated goat antimouse IgG. Specific binding was detected using a 5-bromo-4-chloro-3indolylphosphate (BCIP)/nitroblue tetrazolium (NBT)

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developer system (KPL Inc., Gathersburg, Maryland). In addition, amino-terminal amino acid sequence analysis was carried out on several cleavage products, as described by Luft et al. (Infect. Immun. 57:3637-3645 (1989)). Amido black stained bands were excised from PVDF 30 blots and sequenced by Edman degradation using a Biosystems model 475A sequenator with model 120A PTH analyzer and model 900A control/data analyzer.

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Cleavage Products of Outer Surface Protein A Isolates Purified OspA-B31, labeled with 14C-palmitic acid, was fragmented with hydroxylamine-HCl (HA) into two peptides, designated HA1 and HA2 (data not shown). The HA1 band 5 migrated at 27 KD and retained its radioactivity, indicating that the peptide included the lipidation site at the N-terminus of the molecule (data not shown). From the predicted cleavage point, HA1 should correspond to residues 1 to 251 of OspA-B31. HA2 had a MW of 21.6 KD by SDS-PAGE, 10 with amino-terminal sequence analysis showing it to begin at Gly72, i.e. residues 72 to 273 of OspA-B31. By contrast, HA cleaved OspA-K48 into three peptides, designated HA1, HA2, and HA3 with apparent MWs of 22KD, 16 KD and 12 KD, respectively. Amino-terminal sequencing 15 showed HA1 to start at Gly72, and HA3 at Gly142. HA2 was found to have a blocked amino-terminus, as was observed for the full-length OspA protein. HA1, 2 and 3 of OspA-K48 were predicted to be residues 72-274, 1 to 141 and 142 to 274, respectively.

N-Chlorosuccinimide (NCS) cleaves tryptophan (W), which is at residue 216 of OspA-B31 or residue 217 of OspA-K48 (data not shown). NCS cleaved OspA-B31 into 2 fragments, NCS1, with MW of 23 KD, residues 1-216 of the protein, and NCS2 with a MW of 6.2 KD, residues 217 to 273 25 (data not shown). Similarly, K48 OspA was divided into 2 pieces, NCS1 residues 1-217, and NCS2 residues 218 to 274 (data not shown).

Cleavage of OspA by cyanogen bromide (CNBr) occurs at the carboxy side of methionine, residue 39. The major 30 fragment, CNBr1, has a MW of 25.7 KD, residues 39-274 by amino-terminal amino acid sequence analysis (data not shown). CNBr2 (about 4 KD) could not be visualized by amido black staining; instead, lightly stained bands of about 20 KD MW were seen. These bands reacted with anti-

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OspA MAbs, and most likely were degradation products due to cleavage by formic acid.

Determination of Antibody Binding Domains for Anti-OspA Monoclonal Antibodies

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The cleavage products of OspA-B31 and OspA-K48 were analyzed by Western blot to assess their ability to bind to the six different MAbs. Preliminary Western blot analysis of the cleavage products demonstrated that strains K48 and DK29 have similar patterns of reactivity, as do IP3, PGau 10 and PKo. The OspA of strain PTrob was immunologically distinct from the others, being recognized only by MAb 336. MAb 12 recognized only the two North American strains, B31 and 25015. When the isolates were separated into genogroups, it was remarkable that all the MAbs, except MAb 15 12, crossed over to react with multiple genogroups.

MAb12, specific for OspA-B31, bound to both HA1 and HA2 of OspA-B31. However, cleavage of OspA-B31 by NCS at residue Trp216 created fragments which did not react with MAb12, suggesting that the relevant domain is near or is 20 structurally dependent upon the integrity of this residue (data not shown). MAb 13 bound only to OspA-K48, and to peptides containing the amino-terminus of that molecule (e.g. HA2; NCS1). It did not bind to CNBr1 residues 39 to Thus the domain recognized by MAb13 is in the amino-25 terminal end of OspA-K48, near Met38.

MAb15 reacts with the OspA of both the B31 and K48 strains, and to peptides containing the N-terminus of OspA, such as HA1 of OspA-B31 and NCS1, but not to peptides HA2 of OspA-B31 and HA1 of OspA-K48 (data not shown). Both 30 peptides include residue 72 to the C-terminus of the molecules. MAb15 bound to CNBr1 of OspA-K48, indicating the domain for this antibody to be residues 39 to 72, specifically near Gly72 (data not shown).

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MAD83 binds to OspA-K48, and to peptides containing the C-terminal portion of the molecule, such as HA1. They do not bind to HA2 of OspA-K48, most likely because the C-terminus of HA2 of OspA-K48 ends at 141. Similar to MAD12 and OspA-B31, binding of MADs 83 and CIII.78 is eliminated by cleavage of OspA at the tryptophan residue. Thus binding of MADs 12, 83 and CIII.78 to OspA depends on the structural integrity of the Trp216 residue, which appears to be critical for antigenicity. Also apparent is that, although these MADs bind to a common antigenic domain, the precise epitopes which they recognize are distinct from one another given the varying degrees of cross-reactivity to these MADs among strains.

Although there is similar loss of binding activity of

MAb336 with cleavage at Trp216, this MAb does not bind to

HA1 of OspA-B31, suggesting the domain for this antibody

includes the carboxy-terminal end of the molecule,

inclusive of residues 251 to 273. Low MW peptides, such as

HA3 (10 KD) and NCS2 (6KD), of OspA-K48 do not bind this

MAb on Western blots. In order to confirm this

observation, we tested binding of the 6 MAbs with a

recombinant fusion construct p3A/EC that contains a trpE

leader protein fused with residues 217 to 273 of OspA-B31

(Schubach, W.H. et al., Infect. Immun. 59(6): 1911-1915

(1991)). Only MAb336 reacted with this construct (data not shown). Peptides and antigenic domains localized by

fragmentation of OspA are summarized in Figure 1.

Mapping of Domains to Define the Molecular Basis for the Serotype Analysis

To define the molecular basis for the serotype analysis of OspA, we compared the derived amino acid sequences of OspA for the nine isolates (Figure 2). At the amino terminus of the protein, these predictions can be more precise given the relatively small number of amino

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acid substitutions in this region compared to the carboxy terminus. Domain 1, which is recognized by MAb13, includes residues Leu34 to Leu41. MAb13 only binds to the OspA of species K48, DK29 and IP90. Within this region, residue 37 5 is variable, however Gly37 is conserved amongst the three reactive strains. When Gly37 is changed to Glu37, as it is in OspA of strains B31, pTrob, PGau, and PKo, MAb13 does not recognize the protein (data not shown). By similar analysis, it can be seen that Asp70 is a crucial residue 10 for Domain 2, which includes residues 65 to 75 and is recognized by MAb15. Domain 3 is reactive with MAbs H5332, 12 and 83, and includes residues 190-220. It is clear that significant heterogeneity exists between MAbs reactive with this domain, and that more than one conformational epitope 15 must be contained within the sequence. Domain 4 binds MAb336, and includes residues 250 to 270. In this region, residue 266 is variable and therefore may be an important determinant. It is apparent, however, that other determinants of the reactivity of this monoclonal antibody 20 reside in the region comprising amino acids 217-250. Furthermore, the structural integrity of Trp216 is essential for antibody reactivity in the intact protein. Finally, it is important to stress that Figure 2 indicates only the locations of the domains, and does not necessarily 25 encompass the entire domain. Exact epitopes are being analyzed by site-directed mutagenesis of specific residues.

Overall, evidence suggests that the N-terminal portion is not the immunodominant domain of OspA, possibly by virtue of its lipidation, and the putative function of the lipid moiety in anchoring the protein to the outer envelope. The C-terminal end is immunodominant and includes domains that account in part for structural heterogeneity (Wilske, B. et al., Med. Microbiol. Immunol. 181: 191-207 (1992)), and may provide epitopes for antibody

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neutralization (Sears, J.E. et al., <u>J. Immunol.</u> 147(6):
1995-2000 (1991)), and relate to other activities, such as
the induction of T-cell proliferation (Shanafel, M.M., et
al., <u>J. Immunol.</u> 148: 218-224 (1992)). There are common
epitopes in the carboxy-end of the protein that are shared
among genospecies which may have immunoprotective potential
(Wilske, B., et al., <u>Med. Microbiol. Immunol.</u> 181: 191-207
(1992)).

Prediction of secondary structure on the basis of

hydropathy analysis and circular dichroism and fluorescence spectroscopy measurements (McGrath, B.C., et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York; pp. 365-370 (1993)) suggest domains 3 and 4 to be in a region of the molecule with a propensity to form alphabelix, whereas domains 1 and 2 occur in regions predicted to be beta-sheets (see Figure 1). These differences may distinguish domains in accessibility to antibody or to reactive T-cells (Shanafel, M.M. et al., J. Immunol. 148: 218-224 (1992)). Site-directed mutagenesis of specific epitopes, as described below in Example 2, aids in identifying exact epitopes.

# Example 2. Identification of an Immunologically Important Hypervariable Domain of the Major Outer Surface Protein A of Borrelia

This Example describes epitope mapping studies using chemically cleaved OspA and TrpE-OspA fusion proteins. The studies indicate a hypervariable region surrounding the single conserved tryptophan residue of OspA (at residue 216, or in some cases 217), as determined by a moving window population analysis of OspA from fifteen European and North American isolates of Borrelia. The hypervariable region is important for immune recognition.

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Site-directed mutagenesis was also conducted to examine the hypervariable regions more closely. Fluorescence and circular dichroism spectroscopy have indicated that the conserved tryptophan is part of an 5 alpha-helical region in which the tryptophan is buried in a hydrophobic environment (McGrath, B.C., et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York; pp. 365-370 (1993)). More polar amino acid side-chains flanking the tryptophan are likely to be exposed to the 10 hydrophilic solvent. The hypervariability of these solvent-exposed residues among the various strains of Borrelia suggested that these amino acid residues may contribute to the antigenic variation in OspA. site-directed mutagenesis was performed to replace some of 15 the potentially exposed amino acid side chains in the protein from one strain with the analogous residues of a second strain. The altered proteins were then analyzed by Western Blot using monoclonal antibodies which bind OspA on the surface of the intact, non-mutated spirochete. 20 results indicated that certain specific amino acid changes near the tryptophan can abolish reactivity of OspA to these monoclonal antibodies.

#### Verification of Clustered Polymorphisms in Outer <u>A.</u> Surface Protein A Sequences

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Cloning and sequencing of the OspA protein from fifteen European and North American isolates (described above in Table I) demonstrated that amino acid polymorphism is not randomly distributed throughout the protein; rather, polymorphism tended to be clustered in three regions of The analysis was carried out by plotting the moving, 30 OspA. weighted average polymorphism of a window (a fixed length subsection of the total sequence) as it is slid along the sequence. The window size in this analysis was thirteen amino acids, based upon the determination of the largest

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number of significantly deviating points as established by the method of Tajima (<u>J. Mol. Evol. 33</u>: 470-473 (1991)). The average weighted polymorphism was calculated by summing the number of variant alleles for each site. Polymorphism 5 calculations were weighted by the severity of amino acid replacement (Dayhoff, M.O. et al., in: Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure NBRF, Washington, Vol. 5, Suppl. 3: 345 (1978)). The sum was normalized by the window size and plotted. The amino acid sequence 10 position corresponds to a window that encompasses amino acids 1 through 13. Bootstrap resampling was used to generate 95% confidence intervals on the sliding window analysis. Since Borrelia has been shown to be clonal, the bootstrap analysis should give a reliable estimate of the 15 expected variance out of polymorphism calculations. bootstrap was iterated five hundred times at each position, and the mean was calculated from the sum of all positions. The clonal nature of Borrelia ensures that the stochastic variance that results from differing genealogical histories 20 of the sequence positions (as would be expected if recombination were prevalent) will be minimized.

This test verified that the three regions around the observed peaks all have significant excesses of polymorphism. Excesses of polymorphism were observed in the regions including amino acid residues 132-145, residues 163-177, and residues 208-221 (Figure 3). An amino acid alignment between residues 200 and 220 for B31, K48 and the four site-directed mutants is shown in Figure 4. The amino acid 208-221 region includes the region of OspA which has been modeled as an oriented alpha-helix in which the single tryptophan residue at amino acid 216 is buried in a hydrophobic pocket, thereby exposing more polar amino acids to the solvent (Figure 5) (France, L.L., et al., Biochem. Biophys. Acta 1120: 59 (1992)). These potentially solvent-exposed residues showed considerable variability among the

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OspAs from various strains and may be an important component of OspA antigenic variation. For the purposes of generating chimeric proteins, the hypervariable domains of interest are <u>Domain A</u>, which includes amino acid residues 120-140 of OspA; <u>Domain B</u>, which includes residues 150-180; and <u>Domain C</u>, which includes residues 200-216 or 217.

- B. Site-Directed Mutagenesis of the Hypervariable Region
  Site-directed mutagenesis was performed to convert
  residues within the 204-219 domain of the recombinant B31

  10 OspA to the analogous residues of a European OspA variant,
  K48. In the region of OspA between residues 204 and 219,
  which includes the helical domain (amino acids 204-217),
  there are seven amino acid differences between OspA-B31 and
  OspA-K48. Three oligonucleotides were generated, each
  15 containing nucleotide changes which would incorporate K48
  amino acids at their analogous positions in the B31 OspA
  protein. The oligos used to create the site-directed
  mutants were:
- 5'-CTTAATGACTCTGACACTAGTGC-3' (#613, which converts

  threonine at position 204 to serine, and serine at 206 to
  threonine (Thr204-Ser, Thr206-Ser)) (SEQ ID NO. 1);

  5'-GCTACTAAAAAAACCGGGAAATGGAATTCA-3' (#625, which converts
  alanine at 214 to glycine, and alanine at 215 to lysine
  (Ala214-Gly, Ala215-Lys)) (SEQ ID NO. 2); and
  - 5'-GCAGCTTGGGATTCAAAAACATCCACTTTAACA-3' (#640, which converts asparagine at 217 to aspartate, and glycine at 219 to lysine (Asn217-Asp, Gly219-Lys)) (SEQ ID NO. 3).

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Site-directed mutagenesis was carried out by performing mutagenesis with pairs of the above oligos.

Three site-directed mutants were created, each with two changes: OspA 613 (Thr204-Ser, Thr206-Ser), OspA 625 (Ala214-Gly, Ala215-Lys), and 640 (Asn217-Asp, Gly219-Lys). There were also two proteins with four changes: OspA 613/625 (Thr204-Ser, Thr206-Ser, Ala214-Gly, Ala215-Lys)

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and OspA 613/640 (Thr204-Ser, Thr206-Ser, Asn217-Asp, Gly219-Lys).

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Specificity of Antibody Binding to Epitopes of the Non-mutated Hypervariable Region

Monoclonal antibodies that agglutinate spirochetes, including several which are neutralizing in vitro, recognize epitopes that map to the hypervariable region around Trp216 (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983); Schubach, W.H. et al., <u>Infect. and Immun. 59</u>: 10 1911 (1991)). Western Blot analysis demonstrated that

chemical cleavage of OspA from the B31 strain at Trp 216 abolishes reactivity of the protein with the agglutinating Mab 105, a monoclonal raised against B31 spirochetes (data not shown). The reagent, n-chlorosuccinimide (NCS),

15 cleaves OspA at the Trp 216, forming a 23.2kd fragment and a 6.2kd peptide which is not retained on the Imobilon-P membrane after transfer. The uncleaved material binds Mab 105; however, the 23.2kd fragment is unreactive. Similar Western blots with a TrpE-OspA fusion protein containing

20 the carboxy-terminal portion of the OspA protein demonstrated that the small 6.2kd piece also fails to bind Mab 105 (Schubach, W.H. et al., Infect. and Immun. 59: 1911 (1991)).

Monoclonal antibodies H5332 and H3TS (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983)) have been shown by immunofluorescence to decorate the surface of fixed spirochetes (Wilske, B. et al., World J. Microbiol. 7: 130 (1991)). These monoclonals also inhibit the growth of the organism in culture. Epitope mapping with fusion proteins 30 has confirmed that the epitopes which bind these Mabs are conformationally determined and reside in the carboxy half of the protein. Mab H5332 is cross-reactive among all of the known phylogenetic groups, whereas Mab H3TS and Mab 105 seem to be specific to the B31 strain to which they were

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raised. Like Mab 105, the reactivities of H5332 and H3TS to OspA are abrogated by fragmentation of the protein at Trp216 (data not shown). Mab 336 was raised to whole spirochetes of the strain P/Gau. It cross-reacts to OspA from group 1 (the group to which B31 belongs) but not to group 2 (of which K48 is a member). Previous studies using fusion proteins and chemical cleavage have indicated that this antibody recognizes a domain of OspA in the region between residues 217 and 273 (data not shown). All of these Mabs will agglutinate the B31 spirochete.

Western Blot Analysis of Antibody Binding to Mutated Hypervariable Regions

Mabs were used for Western Blot analysis of the sitedirected OspA mutants induced in E.coli using the T7

15 expression system (Dunn, J.J. et al., Protein Expression
and Purification 1: 159 (1990)). E. coli cells carrying
Pet9c plasmids having a site-directed OspA mutant insert
were induced at mid-log phase growth with IPTG for four
hours at 37°C. Cell lysates were made by boiling an
20 aliquot of the induced cultures in SDS gell loading dye,
and this material was then loaded onto a 12% SDS gell
(BioRad mini-Protean II), and electrophoresed. The
proteins were then transferred to Imobilon-P membranes
(Millipore) 70V, 2 hour at 4°C using the BioRad mini
transfer system. Western analysis was carried out as
described by Schubach et al. (Infect. Immun. 59: 1911
(1991)).

Western Blot analysis indicated that only the 625 mutant (Ala214-Gly and Ala215-Lys) retained binding to the agglutinating monoclonal H3TS (data not shown). However, the 613/625 mutant which has additional alterations to the amino terminus of Trp216 (Ser204-Thr and Thr206-Ser) did not bind this monoclonal. Both 640 and 613/640 OspAs which have the Asn217-Asp and Gly219-Lys changes on the carboxy-

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terminal side of Trp216 also failed to bind Mab H3TS. indicated that the epitope of the B31 OspA which binds H3TS is comprised of amino acid side-chains on both sides of Trp216.

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The 613/625 mutant failed to bind Mabs 105 and H5332, while the other mutants retained their ability to bind these Mabs. This is important in light of the data using fusion proteins that indicate that Mab 105 behaves more like Mab H3TS in terms of its serotype specificity and 10 binding to OspA (Wilske, B. et al., Med. Microbiol. Immunol. 181: 191 (1992)). The 613/625 protein has, in addition to the differences at residues Thr204 and Ser206, changes immediately amino-terminal to Trp216 (Ala214-Gly and Ala215-Lys). The abrogation of reactivity of Mabs 105 and H5332 to this protein indicated that the epitopes of OspA which bind these monoclonals are comprised of residues on the amino-terminal side of Trp216.

The two proteins carrying the Asn217-Asp and Gly219-Lys replacements on the carboxy-terminal side of Trp216 20 (OspAs 640 and 613/640) retained binding to Mabs 105 and H5332; however, they failed to react with Mab 336, a monoclonal which has been mapped with TrpE-OspA fusion proteins and by chemical cleavage to a more carboxyterminal domain. This result may explain why Mab 336 25 failed to recognize the K48-type of OspA (Group 2).

It is clear that amino acids Ser204 and Thr206 play an important part in the agglutinating epitopes in the region of the B31 OspA flanking Trp216. Replacement of these two residues altered the epitopes of OspA that bind Mabs 105, 30 H3TS and H5332. The ability of the 640 changes alone to abolish reactivity of Mab 336 indicated that Thr204 and Ser206 are not involved in direct interaction with Mab 336.

The results indicated that the epitopes of OspA which are available to Mabs that agglutinate spirochetes are 35 comprised at least in part by amino acids in the immediate

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vicinity of Trp216. Since recent circular dichroism analysis indicated that the structures of B31 and K48 OspA differ very little within this domain, it is unlikely that the changes made by mutation have radically altered the overall structure of the OspA protein (France, L.L. et al., Biochem. Biophys. Acta 1120: 59 (1992); and France et al., Biochem. Biophys Acta, submitted (1993)). This hypothesis is supported by the finding that the recombinant, mutant OspAs exhibit the same high solubility and purification properties as the parent B31 protein (data not shown).

In summary, amino acid side-chains at Ser204 and Thr206 are important for many of the agglutinating epitopes. However, a limited set of conservative changes at these sites were not sufficient to abolish binding of all of the agglutinating Mabs. These results suggested that the agglutinating epitopes of OspA are distinct, yet may have some overlap. The results also supported the hypothesis that the surface-exposed epitope around Trp216 which is thought to be important for immune recognition and neutralization is a conformationally-determined and complex domain of OspA.

#### EXAMPLE 3. Borrelia Strains and Proteins

Proteins and genes from any strain of Borrelia can be utilized in the current invention. Representative strains are summarized in Table I, above.

#### A. Genes Encoding Borrelia Proteins

The chimeric peptides of the current invention can comprise peptides derived from any Borrelia proteins.

Representative proteins include OspA, OspB, OspC, OspD,

p12, p39, p41 (fla), p66, and p93. Nucleic acid sequences encoding several Borrelia proteins are presently available (see Table II, below); alternatively, nucleic acid

sequences encoding Borrelia proteins can be isolated and characterized using methods such as those described below.

Table II. References for Nucleic Acid Sequences for Several Proteins of Various Borrelia Strains

Strai	p93	OspA	p41 (fla)
K48	X69602 (SID 67)	X62624 (SID 8)	X69610 (SID 49)
PGau	SID 73	X62387 (SID 10)	X69612 (SID 51)
DK29	-	X63412 (SID 137)	X69608 (SID 53)
PKo	X69803 (SID 77)	X65599 (SID 141)	X69613 (SID 131)
PTrob	X69604 (SID 71)	X65598 (SID 135)	X69614 (SID 55)
Ip3	-	X70365 (SID 140)	-
Ip90	ND	Kryuchechnikov, V.N. et al., <u>J.Microbiol.</u> Epid. Immunobiol. 12:41-44 (1988) (SID 138)	-
25015	X70365 (SID 75)	Fikrig, E.S. et al., <u>J. Immunol. 7</u> :2256- 2260 1992) SID 12)	
B31	Perng, G.C. et al., <u>Infect.</u> <u>Immun. 59:</u> 2070- 74 (1992); Luft, B.J. et al., <u>Infect.</u> <u>Immun. 60:</u> 4309- 4321 (1992) (SID 65)	Bergstrom, S. et al., Mol. Microbiol. 3:479-486 (1989) (SID 6)	Gassmann, G.S. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 3590 (1989) (SID 127)
PKa1		X69606 (SID 132)	X69611 (SID 129)
ZS7	-	Jonsson, M. et al., <u>Infect. Immun.</u> <u>60</u> :1845-1853 (1992) (SID 134)	-
N40	-	Kryuchechnikov, V.N. et al. (SID 133)	-
PHei	-	X65600 (SID 136)	-
ACAI	-	Kryuchechnikov, V.N. et al. (SID 142)	-
РВо	X69601 (SID 69)	X65605 (SID 139)	X69610 (SID 130)

Numbers with an "X" prefix are GenBank data base accession numbers. SID = SEQ ID NO.

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### B. <u>Isolation of Borrelia Genes</u>

Nucleic acid sequences encoding full length, lipidated proteins from known Borrelia strains were isolated using the polymerase chain reaction (PCR) as described below. In 5 addition, nucleic acid sequences were generated which encoded truncated proteins (proteins in which the lipidation signal has been removed, such as by eliminating the nucleic acid sequence encoding the first 18 amino acids, resulting in non-lipidated proteins). Other 10 proteins were generated which encoded polypeptides of a particular gene (i.e., encoding a segment of the protein which has a different number of amino acids than the protein does in nature). Using similar methods as those described below, primers can be generated from known 15 nucleic acid sequences encoding Borrelia proteins and used to isolate other genes encoding Borrelia proteins. Primers can be designed to amplify all of a gene, as well as to amplify a nucleic acid sequence encoding truncated protein sequences, such as described below for OspC, or nucleic 20 acid sequences encoding a polypeptide derived from a Borrelia protein. Primers can also be designed to incorporate unique restriction enzyme cleavage sites into the amplified nucleic acid sequences. Sequence analysis of the amplified nucleic acid sequences can then be performed 25 using standard techniques.

> Cloning and Sequencing of OspA Genes and Relevant Nucleic Acid Sequences

Borrelia OspA sequences were isolated in the following manner: 100 μl reaction mixtures containing 50 mM KCl, 10 mM TRIS-HCl (pH 8,3), 1.5 mM MgCl<sub>2</sub>, 200 μM each NTP, 2.5 units of TaqI DNA polymerase (Amplitaq, Perkin-Elmer/Cetus) and 100 pmol each of the 5' and 3' primers (described below) were used. Amplification was performed in a Perkin-Elmer/Cetus thermal cycler as described (Schubach, W.H. et

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al., Infect. Immun. 59:1811-1915 (1991)). The amplicon was visualized on an agarose gel by ethidium bromide staining. Twenty nanograms of the chloroform-extracted PCR product were cloned directly into the PC-TA vector (Invitrogen) by following the manufacturer's instructions. Recombinant colonies containing the amplified fragment were selected, the plasmids were prepared, and the nucleic acid sequence of each OspA was determined by the dideoxy chain-termination technique using the Sequenase kit (United States Biochemical). Directed sequencing was performed with M13 primers followed by OspA-specific primers derived from sequences, previously obtained with M13 primers.

Because the 5' and 3' ends of the OspA gene are highly conserved (Fikrig, E.S. et al., J. Immunol. 7:2256-2260

15 (1992); Bergstrom, S. et al., Mol. Microbiol. 3: 479-486 (1989); Zumstein, G. et al., Med. Microbiol. Immunol. 181: 57-70 (1992)), the 5' and 3' primers for cloning can be based upon any known OspA sequences. For example, the following primers based upon the OspA nucleic acid sequence from strain B31 were used:

5'-GGAGAATATATTATGAAA-3' (-12 to +6) (SEQ ID NO. 4); and 5'-CTCCTTATTTTAAAGCG-3' (+826 to +809) (SEQ ID NO. 5). (Schubach, W.H. et al., <u>Infect. Immun 59</u>:1811-1915 (1991)).

OspA genes isolated in this manner include those for strains B31, K48, PGau, and 25015; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 6 (OspA-B31), SEQ ID NO. 8 (OspA-K48), SEQ ID NO. 10 (OspA-PGau), and SEQ ID NO. 12 (OspA-25015). An alignment of these and other OspA nucleic acid sequences is shown in Figure 42. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 7 (OspA-B31), SEQ ID NO. 9 (OspA-K48), SEQ ID NO. 11 (OspA-PGau), and SEQ ID NO. 13 (OspA-25015).

The following primers were used to generate specific nucleic acid sequences of the OspA gene, to be used to

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generate chimeric nucleic acid sequences (as described in Example 4):

- 5'-GTCTGCAAAAACCATGACAAG-3' (plus strand primer #369) (SEQ ID NO. 14);
- 5 5'-GTCATCAACAGAAGAAAATTC-3' (plus strand primer #357) (SEQ ID NO 15);
  - 5'-CCGGATCCATATGAAAAAATATTTATTGGG-3' (plus strand primer #607) (SEQ ID NO. 16);
  - 5'-CCGGGATCCATATGGCTAAGCAAAATGTTAGC-3' (plus strand primer
- 10 #584) (SEQ ID NO. 17);

20

- 5'-GCGTTCAAGTACTCCAGA-3' (minus strand primer #200) (SEQ ID NO. 18);
- 5'-GATATCTAGATCTTATTTTAAAGCGTT-3' (minus strand primer #586) (SEQ ID NO. 19); and
- 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAT-3' (minus strand primer #1169) (SEQ ID NO. 20).

Cloning and Sequencing of OspB

Similar methods were also used to isolate OspB genes. One OspB genes isolated is represented as SEQ ID NO. 21 (OspB-B31); its encoded amino acid sequence is SEQ ID NO. 22.

The following primers were used to generate specific nucleic acid sequences of the OspB gene, to be used in generation of chimeric nucleic acid sequences (see Example

- 25 4):
  5'-GGTACAATTACAGTACAA-3' (plus strand primer #721) (SEQ ID
  NO. 23);
  - 5'-CCGAGAATCTCATATGGCACAAAAAGGTGCTGAGTCAATTGG-3' (plus strand primer #1105) (SEQ ID NO. 24);
- 5'-CCGATATCGGATCCTATTTTAAAGCGTTTTTAAGC-3' (minus strand primer # 1106) (SEQ ID NO. 25); and 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAG-3' (minus strand primer #1170) (SEQ ID NO. 26).

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Cloning and Sequencing of OspC

Similar methods were also used to isolate OspC genes. The following primers were used to isolate entire OspC genes from *Borrelia* strains B31, K48, PKO, and pTrob:

5'-GTGCGCGACCATATGAAAAAGAATACATTAAGTGCG-3' (plus strand primer having Ndel site combined with start codon) (SEQ ID NO. 27), and

5'-GTCGGCGGATCCTTAAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer having BamH1 site followed by stop codon) (SEQ ID NO. 28).

The nucleic acid sequences of the OspC genes were then determined by the dideoxy chain-termination technique using the Sequenase kit (United States Biochemical). OspC genes isolated and sequenced in this manner include those for strains B31, K48, PKo, and Tro; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 29 (OspC-B31), SEQ ID NO. 31 (OspC-K48), SEQ ID NO. 33 (OspC-PKo), and SEQ ID NO. 35 (OspC-Tro). An alignment of these sequences is shown in Figure 38. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 30 (OspC-B31), SEQ ID NO. 32 (OspC-K48), SEQ ID NO. 34 (OspC-PKo), and SEQ ID NO. 36 (OspC-Tro).

Truncated OspC genes were generated using other

25 primers. These primers were designed to amplify nucleic acid sequences, derived from the OspC gene, that lacked the nucleic acids encoding the signal peptidase sequence of the full-length protein. The primers corresponded to bp 58-75 of the natural protein, with a codon for Met-Ala attached

30 ahead. For strain B31, the following primer was used:

5'-GTGCGCGACCATATGGCTAATAATTCAGGGAAAGAT-3' (SEQ ID NO. 37).

For strain PKo,

5'-GTGCGCGACCATATGGCTAGTAATTCAGGGAAAGGT-3' (SEQ ID NO. 38)
35 was used.

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For strains pTrob and K48, 5'-GTGCGCGACCATATGGCTAATAATTCAGGTGGGGAT-3' (SEQ ID NO. 39) was used.

Additional primers were also designed to amplify

nucleic acids encoding particular polypeptides, for use in
creation of chimeric nucleic acid sequences (see Example
4). These primers included:

5'-CTTGGAAAATTATTTGAA-3' (plus strand primer #520) (SEQ ID NO. 40);

5'-CACGGTCACCCCATGGGAAATAATTCAGGGAAAGG-3' (plus strand
primer #58) (SEQ ID NO. 41);

5'-TATAGATGACAGCAACGC-3' (minus strand primer #207) (SEQ ID NO. 42); and

5'-CCGGTGACCCCATGGTACCAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer #636) (SEQ ID NO. 43).

Cloning and Sequencing of OspD

Similar methods can be used to isolate OspD genes. An alignment of four OspD nucleic acid sequences (from strains pBo, PGau, DK29, and K48) is shown in Figure 39.

20 Cloning and Sequencing of p12

The p12 gene was similarly identified. Primers used to clone the entire p12 gene included: 5'CCGGATCCATATGGTTAAAAAAATAATATTTATTTC-3' (forward primer # 757) (SEQ ID NO. 44); and 5'-

25 GATATCTAGATCTTTAATTGCTCTGCTCACTCTCTTC-3' (reverse primer #758) (SEQ ID NO. 45).

To amplify a truncated p12 gene (one in which the transcribed protein is non-lipidated, and begins at amino acid 18 of the native sequence), the following primers were used: 5'-CCGGGATCCATATGGCTAGTGCAATTGGTCGTGG-3' (forward primer # 759) (SEQ ID NO. 46); and primer #758 (SEQ ID NO. 45).

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Cloning and Sequencing of p41 (fla)

A similar approach was used to clone and sequence genes encoding the p41 (fla) protein. The p41 sequences listed in Table II with GenBank accession numbers were 5 isolated using the following primers from strain B31: 5'-ATGATTATCAATCATAAT-3' (+1 to +18) (SEQ ID NO. 47); and 5'-TCTGAACAATGACAAAAC-3' (+1008 to +991) (SEQ ID NO. 48). The nucleic acid sequences of p41 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 51 (p41-10 PGau), and SEQ ID NO. 53 (p41-DK29). An alignment of several p41 nucleic acid sequences, including those for strains B31, pKa1, PGau, pBo, DK29, and pKo, is shown in Figure 41. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as 15 SEQ ID NO. 50 (p41-K48), SEQ ID NO. 52 (p41-PGau), SEQ ID NO. 54 (p41-DK29), SEQ ID NO. 56 (p41-PTrob), and SEQ ID NO. 58 (p41-PHei).

Other primers were designed to amplify nucleic acid sequences encoding polypeptides of p41, to be used in chimeric nucleic acid sequences. These primers included: 5'-TTGGATCCGGTCACCCCATGGCTCAATATAACCAATG-3' (minus strand primer #122) (SEQ ID NO. 59);

5'-TTGGATCCGGTCACCCCATGGCTTCTCAAAATGTAAG-3' (plus strand primer # 140) (SEQ ID NO. 60);

5'-TTGGATCCGGTGACCAACTCCGCCTTGAGAAGG-3' (minus strand primer # 234) (SEQ ID NO. 61); and 5'-TTGGATCCGGTGACCTATTTGAGCATAAGATGC-3' (minus strand primer #141) (SEQ ID NO. 62).

Cloning and Sequencing of p93

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The same approach was also used to clone and sequence p93 protein. Genes encoding p93, as listed in Table II with GenBank accession numbers, were isolated by this method with the following primers from strain B31:

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5'-GGTGAATTTAGTTGGTAAGG-3' (-54 to -35) (SEQ ID NO. 63);

5'-CACCAGTTTCTTTAAGCTGCTCCTGC-3' (+1117 to +1092) (SEQ ID NO. 64).

The nucleic acid sequences of p93 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 65 (p93-B31), SEQ ID NO. 67 (p93-K48) SEQ ID NO. 69 (p93-PBo), SEQ ID NO. 71 (p93-PTrob), SEQ ID NO. 73 (p93-PGau), SEQ ID NO. 75 (p93-25015), and SEQ ID NO. 77 (p93-PKo).

The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 66 (p93-B31), SEQ ID NO. 68 (p93-K48) SEQ ID NO. 70 (p93-PBo), SEQ ID NO. 72 (p93-PTrob), SEQ ID NO. 74 (p93-PGau), SEQ ID NO. 76 (p93-25015), and SEQ ID NO. 78 (p93-PKo).

Other primers were used to amplify nucleic acid sequences encoding polypeptides of p93 to be used in generating chimeric nucleic acid sequences. These primers included:

5'-CCGGTCACCCCATGGCTGCTTTAAAGTCTTTA-3' (plus strand primer 20 #475) (SEQ ID NO. 79);

5'-CCGGTCACCCCATGAATCTTGATAAAGCTCAG-3' (plus strand primer

#900) (SEQ ID NO. 80);
5'-CCGGTCACCCCATGGATGAAAAGCTTTTAAAAAGT-3' (plus strand

primer #1168) (SEQ ID NO. 81);

5'-CCGGTCACCCCCATGGTTGAGAAATTAGATAAG-3' (plus strand
primer #1423) (SEQ ID NO. 82); and

5'-TTGGATCCGGTGACCCTTAACTTTTTTAAAG-3' (minus strand primer # 2100) (SEQ ID NO. 83).

## C. Expression of Proteins from Borrelia Genes

The nucleic acid sequences described above can be incorporated into expression plasmids, using standard techniques, and transfected into compatible host cells in order to express the proteins encoded by the nucleic acid

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sequences. As an example, the expression the pl2 gene and the isolation of pl2 protein is set forth.

Amplification of the pl2 nucleic acid sequence was conducted with primers that included a NdeI restriction 5 site into the nucleic acid sequence. The PCR product was extracted with phenol/chloroform and precipitated with ethanol. The precipitated product was digested and ligated into an expression plasmid as follows: 15  $\mu$ l (approximately 1  $\mu g$ ) of PCR DNA was combined with 2  $\mu l$  10X 10 restriction buffer for NdeI (Gibco/BRL), 1  $\mu$ l NdeI (Gibco/BRL), and 2  $\mu$ l distilled water, and incubated overnight at 37°C. This mixture was subsequently combined with 3  $\mu$ l 10X buffer (buffer 3, New England BioLabs), 1  $\mu$ l BamHI (NEB), and 6  $\mu l$  distilled water, and incubated at 37° 15 for two hours. The resultant material was purified by preparative gel electrophoresis using low melting point agarose, and the band was visualized under long wave ultraviolet light and excised from the gel. The gel slice was treated with Gelase using conditions recommended by the 20 manufacturer (Epicentre Technologies). The resulting DNA pelled was resuspended in 25-50  $\mu l$  of 10 mM TRIS-CL (pH 8.0) and 1 mM EDTA (TE). An aliquot of this material was ligated into the Pet9c expression vector (Dunn, J. J. et al., Protein Expression and Purification 1: 159 (1990)).

To ligate the material into the Pet9c expression vector, 20-50 ng of pl2 nucleic acid sequences cut and purified as described above was combined with 5  $\mu$ l 10 One-Phor-All (OPA) buffer (Pharmacia), 30-60 ng Pet9c cut with NdeI and BamHI, 2.5  $\mu$ l 20 mM ATP, 2  $\mu$ l T4 DNA ligase (Pharmacia) diluted 1:5 in 1% OPA buffer, and sufficient distilled water to bring the final volume to 50  $\mu$ l. The mixture was incubated at 12°C overnight.

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The resultant ligations were transformed into competent DH5-alpha cells and plated on nutrient agar plates containing 50  $\mu g/ml$  kanamycin and incubated

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overnight at 37 °C. DH5-alpha is used as a "storage strain" for T7 expression clones, because it is RecA deficient, so that recombination and concatenation are not problematic, and because it lacks the T7 RNA polymerase gene necessary to express the cloned gene. The use of this strain allows for cloning of potentially toxic gene products while minimizing the chance of deletion and/or rearrangement of the desired genes. Other cell lines having similar properties may also be used.

10 Kanamycin resistant colonies were single-colony purified on nutrient agar plates supplemented with kanamycin at 50  $\mu$ g/ml. A colony from each isolate was inoculated into 3-5 ml of liquid medium containing 50  $\mu$ g/ml kanamycin, and incubated at 37°C without agitation.

Plasmid DNA was obtained from 1 ml of each isolate using a hot alkaline lysis procedure (Mantiatis, T. et al., Molecular Cloning: A Laboratory Manual, cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982)).

Plasmid DNA was digested with EcoRI and BglII in the following manner: 15  $\mu$ l plasmid DNA was combined with 2  $\mu$ l 10X buffer 3 (NEB), 1  $\mu$  EcoRI (NEB), 1  $\mu$ l BglII (NEB) and 1  $\mu$ l distilled water, and incubated for two hours at 37°C. The entire reaction mixture was electrophoresed on an analytical agarose gel. Plasmids carrying the p12 insert were identified by the presence of a band corresponding to 925 base-pairs (full length p12) or 875 base-pairs (nonlipidated p12).

One or two plasmid DNAs from the full length and nonlipidated p12 clones in Pet9c were used to transform

30 BL21 DE3 pLysS to kanamycin resistance as described by Studier et al. (Methods in Enzymology, Goeddel, D. (Ed.), Academic Press, 185: 60-89 (1990)). One or two transformants of the full length and nonlipidated clones were single-colony purified on nutrient plates containing

35 µg/ml chloramphenicol (to maintain pLysS) and 50 µg/ml

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kanamycin at 37 °C. One colony of each isolate was inoculated into liquid medium supplemented with chloramphenicol and kanamycin and incubated overnight at 37°C. The overnight culture was subcultured the following morning into 500 ml of liquid broth with chloramphenicol (25 μg/ml) and kanamycin (50 μg/ml) and grown with aeration at 37°C in an orbital air-shaker until the absorbance at 600 nm reached 0.4-0.7. Isopropyl-thio-galactoside (IPTG) was added to a final concentration of 0.5 mM, for induction, and the culture was incubated for 3-4 hours at 37° as before. The induced cells were pelleted by centrifugation and resuspended in 25 ml of 20 mM NaPO<sub>4</sub> (pH 7.7). A small aliquot was removed for analysis by gel electrophoresis. Expressing clones produced proteins which migrated at the 12 kDa position.

A crude cell lysate was prepared from the culture as described for recombinant OspA by Dunn, J.J. et al., (Protein Expression and Purification 1: 159 (1990)). crude lysate was first passed over a Q-sepharose column 20 (Pharmacia) which had been pre-equilibrated in Buffer A: 10 mM  $\mathrm{NaPO_4}$  (pH 7.7), 10 mM  $\mathrm{NaCl}$ , 0.5 mM  $\mathrm{PMSF}$ . The column was washed with 10 mM NaPO4, 50 mM NaCl and 0.5 mM PMSF and then pl2 was eluted in 10 mM NaPO4, 0.5 mM PMSF with a NaCl gradient from 50-400 mM. pl2 eluted approximately halfway 25 through the gradient between 100 and 200 mM NaCl. The peak fractions were pooled and dialyzed against 10 mM NaPo4 (pH 7.7), 10 mM NaCl, 0.5 mM PMSF. The protein was then concentrated and applied to a Sephadex G50 gel filtration column of approximately 50 ml bed volume (Pharmacia), in 10 30 mM NaPO, 200 mM NaCl, 0.5 mM PMSF. p12 would typically elute shortly after the excluded volume marker. Peak fractions were determined by running small aliquots of all fractions on a gel. The p12 peak was pooled and stored in small aliquots at -20°C.

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#### Generation of Chimeric Nucleic Acid Example 4. Sequences and Chimeric Proteins

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#### General Protocol for Creation of Chimeric Nucleic Acid **A**. Sequences

The megaprimer method of site directed mutagenesis and its modification were used to generate chimeric nucleic acid sequences (Sarkar and Sommer, Biotechniques 8(4): 404-407 (1990); Aiyar, A. and J. Leis, <u>Biotechniques 14(3):</u> 366-369 (1993)). A 5' primer for the first genomic 10 template and a 3' fusion oligo are used to amplify the desired region. the fusion primer consists of a 3' end of the first template (DNA that encodes the amino-proximal polypeptide of the fusion protein), coupled to a 5' end of the second template (DNA that encodes the carboxy-proximal 15 polypeptide of the fusion protein).

The PCR amplifications are performed using Taq DNA polymerase, 10X PCR buffer, and MgCl<sub>2</sub> (Promega Corp., Madison, WI), and Ultrapure dNTPs (Pharmacia, Piscataway, NJ). One  $\mu g$  of genomic template 1, 5  $\mu$  of 10  $\mu M$  5' oligo 20 and 5  $\mu l$  of 10  $\mu M$  fusion oligo are combined with the following reagents at indicated final concentrations: 10X Buffer-Mg FREE (1X), MgCl $_2$  (2 mM), dNTP mix (200  $\mu$ M each dNTP), Taq DNA polymerase (2.5 units), water to bring final volume to 100  $\mu$ l. A Thermal Cycler (Perkin Elmer Cetus,

25 Norwalk, CT) is used to amplify under the following conditions: 35 cycles at 95°C for one minute, 55°C for two minutes, and 72° for three minutes. This procedure results in a "megaprimer".

The resulting megaprimer is run on a 1X TAE, 4% low-30 melt agarose gel. The megaprimer band is cut from the gel and purified using the Promega Magic PCR Preps DNA purification system. Purified megaprimer is then used in a second PCR step. One  $\mu g$  of genomic template 2, approximately 0.5  $\mu g$  of the megaprimer, and 5  $\mu$  of 10  $\mu M$  3'

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oligo are added to a cocktail of 10X buffer, MgCl2, dNTPs and Taq at the same final concentrations as noted above, and brought to 100  $\mu l$  with water. PCR conditions are the same as above. The fusion product resulting from this 5 amplification is also purified using the Promega Magic PCR Preps DNA purification system.

The fusion product is then ligated into TA vector and transformed into E. coli using the Invitrogen (San Diego, CA) TA Cloning Kit. Approximately 50 ng of PCR fusion 10 product is ligated to 50 ng of pCRII vector with 1X Ligation Buffer, 4 units of T4 ligase, and brought to 10 N1 with water. This ligated product mixture is incubated at 12°C overnight (approximately 14 hours). Two  $\mu l$  of the ligation product mixture is added to 50  $\mu l$  competent INC F' 15 cells and 2  $\mu$  beta mercaptoethanol. The cells are then incubated for 30 minutes, followed by heat shock treatment at 42°C for 60 seconds, and an ice quenching for two minutes. 450  $\mu$ l of warmed SOC media is then added to the cells, resulting in a transformed cell culture which is 20 incubated at 37°C for one hour with slight shaking. of the transformed cell culture is plated on LB + 50  $\mu g/\mu l$ ampicillin plates and incubated overnight at 37°C. Single white colonies are picked and added to individual overnight cultures containing 3 ml LB with ampicillin (50  $\mu g/\mu l$ ).

The individual overnight cultures are prepared using Promega's Magic Miniprep DNA purification system. A small amount of the resulting DNA is cut using a restriction digest as a check. DNA sequencing is then performed to check the sequence of the fusion nucleic acid sequence, 30 using the United States Biochemical (Cleveland, OH) Sequenase Version 2.0 DNA sequencing kit. Three to five  $\mu g$ of plasmid DNA is used per reaction. 2  $\mu$ l 2M NaOH/2mM EDTA are added to the DNA, and the volume is brought to 20  $\mu l$ with water. The mixture is then incubated at room 35 temperature for five minutes. 7  $\mu$ l water, 3 $\mu$ l 3M NaAc, 75

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 $\mu$ l EtOH are added. The resultant mixture is mixed by vortex and incubated for ten minutes at -70°C, and then subjected to microfugation. After microfuge for ten minutes, the supernatant is aspirated off, and the pellet 5 is dried in the speed vac for 30 second. 6  $\mu l$  water, 2  $\mu l$ annealing buffer, and 2  $\mu l$  of 10  $\mu M$  of the appropriate oligo is then added. This mixture is incubated for 10 minutes at 37°C and then allowed to stand at room temperature for 10 minutes. Subsequently, 5.5  $\mu$ l of label 10 cocktail (described above) is added to each sample of the mixture, which are incubated at room temperature for an additional five minutes. 3.5  $\mu l$  labeled DNA is then added to each sample which is then incubated for five minutes at 37°C. 4  $\mu$ l stop solution is added to each well. 15 is denatured at 95° for two minutes, and then placed on ice.

Clones with the desired fusion nucleic acid sequences are then recloned in frame in the pEt expression system in the lipidated (full length) and non-lipidated (truncated, 20 i.e., without first 17 amino acids) forms. The product is amplified using restriction sites contained in the PCR primers. The vector and product are cut with the same enzymes and ligated together with T4 ligase. The resultant plasmid is transformed into competent E. coli using 25 standard transformation techniques. Colonies are screened as described earlier and positive clones are transformed into expression cells, such as E. coli BL21, for protein expression with IPTG for induction. The expressed protein in its bacterial culture lysate form and/or purified form 30 is then injected in mice for antibody production. The mice are bled, and the sera collected for agglutination, in vitro growth inhibition, and complement- dependent and independent lysis tests.

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## B. Specific Chimeric Nucleic Acid Sequences

Various chimeric nucleic acid sequences were generated. The nucleic acid sequences are described as encoding polypeptides from Borrelia proteins. The chimeric nucleic acid sequences are produced such that the nucleic acid sequence encoding one polypeptide is in the same reading frame as the nucleic acid sequence encoding the next polypeptide in the chimeric protein sequence encoded by the chimeric nucleic acid sequence. The proteins are listed sequentially (in order of presence of the encoding sequence) in the description of the chimeric nucleic acid sequence. For example, if a chimeric nucleic acid sequence consists of bp 1-650 from OspA-1 and bp 651-820 from OspA-2 were sequenced, the sequence of the chimer would include the first 650 base pairs from OspA-1 followed immediately by base pairs 651-820 of OspA-2.

OspA-K48/OspA-PGau A chimer of OspA from strain
K48 (OspA-K48) and OspA from strain PGau (OspA-PGau) was
generated using the method described above. This chimeric
nucleic acid sequence included bp 1-654 from OspA-K48,
followed by bp 655-820 from OspA-PGau. Primers used
included: the amino-terminal sequence of OspA primer #607
(SEQ ID NO. 16); the fusion primer,

5'-AAAGTAGAAGTTTTTGAATCCCATTTTCCAGTTTTTTT-3' (minus strand primer #668-654) (SEQ ID NO. 84); the carboxy-terminal sequence of OspA primer #586 (SEQ ID NO. 19); and the sequence primers #369 (SEQ ID NO. 14) and #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 85; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 86.

OspA-B31/OspA-PGau A chimer of OspA from strain B31 (OspA-B31) and OspA from strain PGau (OspA-PGau) was generated

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using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-PGau. Primers used included: the fusion primer,

5 5'-AAAGTAGAAGTTTTTGAATTCCAAGCTGCAGTTTT-3' (minus strand primer #668-651) (SEQ ID NO. 87); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence is presented as SEQ ID NO. 88; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 89.

OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-K48. Primers used included: the fusion primer,

primer #671-651) (SEQ ID NO. 90); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence 20 is presented as SEQ ID NO. 91; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 92.

5'-AAAGTGGAAGTTTTTGAATTCCAAGCTGCAGTTTTTTT-3' (minus strand

OspA-B31/OspA-25015 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain 25015 (OspA-25015) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-25015. Primers used included: the fusion primer, 5'-TAAAGTTGAAGTGCCTGCATTCCAAGCTGCAGTTT-3' (SEQ ID NO. 93). The chimeric nucleic acid sequence is presented as SEQ ID NO. 94; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 95.

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OspA-K48/OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-570 from OspA-B31, followed by bp 570-651 from OspA-B31, followed by bp 650-820 from OspA-K48. Primers used included: the fusion primer, 5'-CCCCAGATTTTGAAATCTTGCTTAAAACAAC-3' (SEQ ID NO. 96); and the sequence primer, #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 97; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 98.

OspA-B31/OspA-K48/OspA-B31/OspA-K48

A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-420 from OspA-B31, followed by 420-570 from OspA-K48, followed by bp 570-650 from OspA-B31, followed by bp 651-820 from OspA-K48. Primers used included: the fusion primer, 5'-CAAGTCTGGTTCCAATTTGCTCTTGTTATTAT-3' (minus strand primer #436-420) (SEQ ID NO. 99); and the sequence primer, #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 100; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 101.

OspA-B31/OspB-B31 A chimer of OspA and OspB from strain
B31 (OspA-B31, OspB-B31) was generated using the method
described above. The chimeric nucleic acid sequence
included bp 1-651 from OspA-B31, followed by bp 652-820
from OspB-B31. Primers used included: the fusion primer,
5'-GTTAAAGTGCTAGTACTGTCATTCCAAGCTGCAGTTTTTTT-3' (minus
strand primer #740-651) (SEQ ID NO. 102); the carboxyterminal sequence of OspB primer #1106 (SEQ ID NO. 25); and
the sequence primer #357 (SEQ ID NO. 15). The chimeric

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nucleic acid sequence is presented as SEQ ID NO. 103; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 104.

OspA-B31/OspB-B31/OspC-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-650 from OspA-B31, followed by bp 652-820 from OspB-B31, followed by bp 74-630 of OspC-B31. Primers used included: the fusion primer, 5'-TGCAGATGTAATCCCATCCGCCATTTTTAAAGCGTTTTT-3' (SEQ ID NO. 105); and the carboxy-terminal sequence of OspC primer (SEQ ID NO. 28). The chimeric nucleic acid sequence is presented as SEQ ID NO. 106; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 107.

OspC-B31/OspA-B31/OspB-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-630 from OspC-B31, followed by bp 52-650 from OspA-B31, followed by bp 650-820 of OspB-B31. Primers used included: the amino-terminal sequence of OspC primer having SEQ ID NO. 27; the fusion primer, 5'-GCTGCTAACATTTTGCTTAGGTTTTTTTGGACTTTC-3' (minus strand primer #69-630) (SEQ ID NO. 108); and the sequence primers #520 (SEQ ID NO. 40) and #200 (SEQ ID NO. 18). The chimeric nucleic acid sequence is presented as SEQ ID NO. 109; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 110.

## 30 Additional Chimeric Nucleic Acid Sequences

Using the methods described above, other chimeric nucleic acid sequences were produced. These chimeric

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nucleic acid sequences, and the proteins encoded, are summarized in Table 3.

Table III Chimeric Nucleic acid Sequences and the Encoded Proteins

PIOCEINS		
Chimers Generated (base pairs)	SEQ ID NO. (nt)	SEQ ID NO. (protein)
OspA (52-882) / p93 (1168-2100)	111	112
OspB (45-891) / p41 (122-234)	113	114
OspB (45-891) / p41 (122-295)	115	116
OspB (45-891) / p41 (140-234)	117	118
OspB (45-891) / p41 (140-295)	119	120
OspB (45-891) / p41 (122-234) / OspC (58-633)	121	122
OspA-Tro/OspA-Bo	137	138
OspA-PGau/OspA-Bo	139	140
OspA-B31/OspA-PGau/OspA-B31/ OspA-K48	141	142
OspA-PGau/OspA-B31/OspA-K48	143	144

# C. Purification of Proteins Generated by Chimeric Nucleic Acid Sequences

The chimeric nucleic acid sequences described above, as well as chimeric nucleic acid sequences produced by the methods described above, are used to produce chimeric proteins encoded by the nucleic acid sequences. Standard methods, such as those described above in Example 3, concerning the expression of proteins from Borrelia genes, can be used to express the proteins in a compatible host organism. The chimeric proteins can then be isolated and purified using standard techniques.

If the chimeric protein is soluble, it can be purified on a Sepharose column. Insoluble proteins can be solubilized in guanidine and purified on a Ni++ column;

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alternatively, they can be solubilized in 10 mM NaPO<sub>4</sub> with 0.1 - 1% TRIXON X 114, and subsequently purified over an S column (Pharmacia). Lipidated proteins were generally purified by the latter method. Solubility was determined by separating both soluble and insoluble fractions of cell lysate on a 12% PAGE gel, and checking for the localization of the protein by Coomasie staining, or by Western blotting with monoclonal antibodies directed to an antigenic polypeptide of the chimeric protein.

#### 10 Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. such equivalents are intended to be encompassed in the scope of the following claims.

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#### CLAIMS

What is claimed is:

- A chimeric protein comprising two or more antigenic Borrelia polypeptides, wherein the antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
  - The chimeric protein of Claim 1, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- The chimeric protein of Claim 2, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 4. The chimeric protein of Claim 3, wherein the antigenic Borrelia polypeptides are from corresponding proteins from two or more different species of Borrelia.
- 5. The chimeric protein of Claim 3, wherein the antigenic
  Borrelia polypeptides are from non-corresponding
  proteins from at least two different species of
  Borrelia.
- The chimeric protein of Claim 1, wherein two or more antigenic Borrelia polypeptides are from the same
   species of Borrelia.

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7. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.

- 8. The chimeric protein of Claim 7, wherein the antigenic Borrelia polypeptides are from the same protein.
- 9. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are from different proteins.
- 10. A chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the amino-proximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.
- 20 11. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from the same species of *Borrelia*.
- 12. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
  - 13. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein B, and

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the second outer surface protein is outer surface protein A.

14. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from different species of *Borrelia*.

- 15. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 10 16. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 17. The chimeric protein of Claim 14, wherein the first
  and second outer surface proteins are corresponding
  proteins selected from the group consisting of: outer
  surface protein A and outer surface protein B.
- 18. The chimeric protein of Claim 10, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 19. The chimeric protein of Claim 18, wherein the aminoproximal polypeptide further comprises a first,
  second, and third hypervariable domain, the first
  hypervariable domain consisting of residues 120
  through 140 of outer surface protein A, the second
  hypervariable domain consisting of residues 150
  through 180 of outer surface protein A, and the third

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hypervariable domain consisting of residues 200 through 217 of outer surface protein A.

20. The chimeric protein of Claim 19, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.

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- 21. The chimeric protein of Claim 10, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
- 22. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides,
  wherein the two antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
- 23. The nucleic acid sequence of Claim 22, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
  - 24. The nucleic acid sequence of Claim 23, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
    - 25. The nucleic acid sequence of Claim 24, wherein the antigenic *Borrelia* polypeptides are from corresponding

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proteins from two or more different species of Borrelia.

26. The nucleic acid sequence of Claim 24, wherein two or more of the antigenic Borrelia polypeptides are from non-corresponding proteins from different species of Borrelia.

- 27. The nucleic acid sequence of Claim 22, wherein two or more antigenic Borrelia polypeptides are from the same species of Borrelia.
- The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 29. The nucleic acid sequence of Claim 28, wherein the antigenic *Borrelia* polypeptides are from the same protein.
- 30. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are from different proteins.

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31. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the aminoproximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.

- 10 32. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from the same species of *Borrelia*.
- 33. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 34. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
  - 35. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from different species of *Borrelia*.
- 36. The nucleic acid sequence of Claim 35, wherein the
  25 first outer surface protein is outer surface protein A
  and the second outer surface protein is outer surface
  protein B.

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- 37. The nucleic acid sequence of Claim 35, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 5 38. The nucleic acid sequence of Claim 35, wherein the first and second outer surface proteins are corresponding proteins selected from the group consisting of: outer surface protein A and outer surface protein B.
- 10 39. The nucleic acid sequence of Claim 31, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 40. The nucleic acid sequence of Claim 39, wherein the
  amino-proximal polypeptide further comprises a first
  and a second hypervariable domain, the first
  hypervariable domain consisting of amino acid residues
  1 through 140 of outer surface protein A, and the
  second hypervariable domain consisting of amino acid
  residues 150 through 217 of outer surface protein A.
  - 41. The nucleic acid sequence of Claim 40, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.
- 25 42. The nucleic acid sequence of Claim 31, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.

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43. A nucleic acid sequence having a sequence selected from the group consisting of: SEQ ID NO. 85, SEQ ID NO. 88, SEQ ID NO. 91, SEQ ID NO. 94, SEQ ID NO. 97, SEQ ID NO. 100, SEQ ID NO. 103, SEQ ID NO. 106, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 141, and SEQ ID NO. 143.

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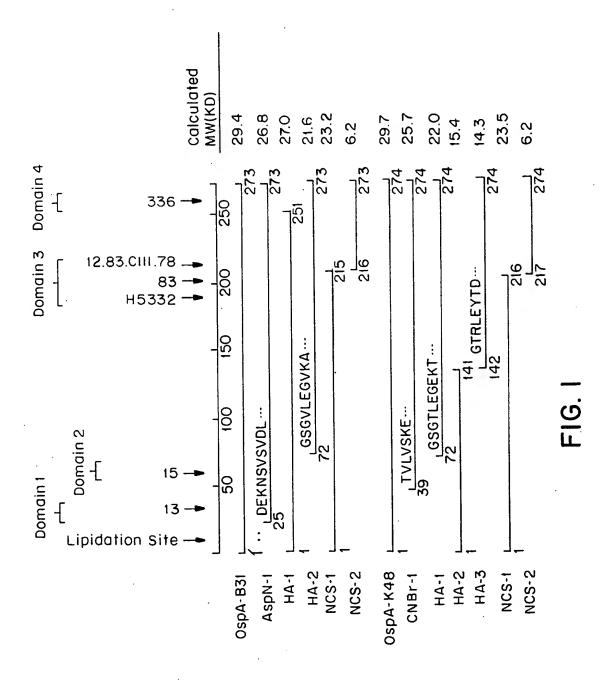
- 44. A protein having an amino acid sequence selected from
  the group consisting of: SEQ ID NO. 86, SEQ ID NO.
  89, SEQ ID NO. 92, SEQ ID NO. 95, SEQ ID NO. 98, SEQ
  ID NO. 101, SEQ ID NO. 104, SEQ ID NO. 107, SEQ ID NO.
  110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116,
  SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID
  NO. 138, SEQ ID NO. 140, SEQ ID NO. 142, and SEQ ID
  NO. 144.
- 45. A chimeric protein according to any one of claims 1 to 21 and 44 for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
  - 46. A chimeric protein according to claim 45, wherein the immunodiagnostic assay is a dot blot, Western blot, ELISA or agglutination assay.

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- 47. Use of the chimeric protein according to any one of claims 1 to 21 and 44, or the nucleic acid sequence of any one of claims 22 to 43, for the manufacture of a compound for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
- 48. Use according to claim 47, wherein the

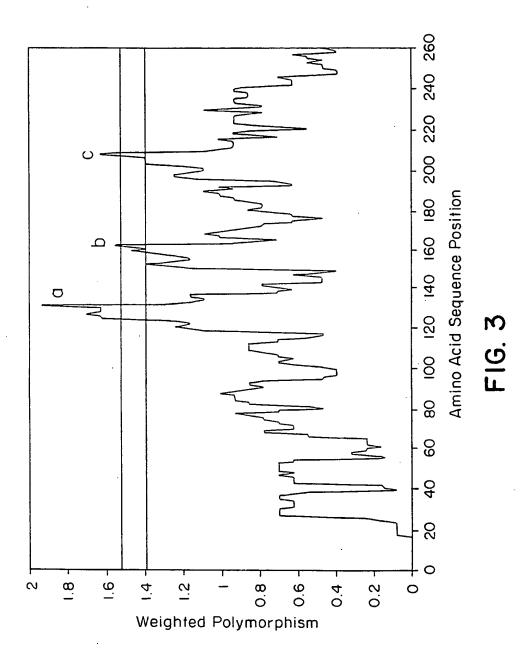
  immunodiagnostic assay is a dot blot, Western blot,

  ELISA or agglutination assay.



				ДÕ	Domain	-								Domain	ain 2	_,				
	34	35	36	37	38	39	40	41		65	99	67	89	69	70	7.1	72	73	74	75
A-B31	H	Д	O	м	Σ	×	>	H	A-B31	ט	H	ß	Ω	×	z	z	v	S	ט	>
A-TRo	า	а	Ö	网	Σ	×	>	7	A-TRO	ט	F	တ	Д	×	တ	z	ט	ຜ	ט	<b>-</b>
A-K48	IJ	Д	Ö	U	Σ	H	>	IJ	A-K48	ტ	H	හ	Ω	×	z	z	U	S	ט	H
A-DK29	'n	Δ,	ŋ	O	Σ	۲	>	ı	A-DK29	ซ	Ħ	Ŋ	Ω	×	z	z	ט	ß	r U	H
A-P/Gau	IJ		Ö	ы	Σ	×	>	ıı	A-P/Gau	O	H	ຜຸ	Д	×	D	z	ט	S	ט	F
A-PKo	H	Д	Ö	田	Σ	×	>	'n	A-PKo	U	H	ຜ	Ω	×	Ω	z	ט	Ø	ט	F
A-IP3	נו	Д	Ö	ធ	н	×	>	1	A-IP3	ט	Ħ	ຜ	Ω	×	Ω	z	ט	S	ַט	>
A-IP90	J.	<b>ሲ</b>	ט	ט	Σ	v	>	בי	A-IP90	ט	H	ഗ	Ω	×	z	z	ט	S	უ	<b>-</b>
A-25015	, LJ	α	U	ш	Σ	×	>	ı,	A-25015	ט	H	cs	Ω	×	z	z	U	S	້	>
			Ω	Domain 3	e E							Domain 4	ln 4							
	190		7	200		210	_	220		250		260		270						
A-B31	NIS	KSGE	SVSV	<b>NISKSGEVSVELNDTDSSAATKKTAAWNSGT</b>	TDSS	VATKK	TAAK	NSGT	A-B31	SNGTKLEGSAVEITKLDEIKN	LEGS	AVEI	rkldi	SIKN						
A-TRO	HIF	NSGE	TITA	hipnsgeitvelndsnstqatkktgkwdsnt	SNSTÇ	<b>ZATKK</b>	TGKE	TNSOT	A-TRO	SAGINLEGNAVEIKTLDELKN	LEGN	AVEI	KTLDI	SLKN						
A-K48	NII	KSGE	IIV	NILKSGEITVALDDSDTTQATKKTGKWDSKT	SDTTÇ	ATKK	TGK	DSKT	A-K48	SAGINLEGKAVEITILKELKN	LEGK	AVEI	FTLK	SLKN						
A-DK29	NII	KSGE	TITA	ALDD	SDTT	WTKK	TGK	DSKT	A-DK29	SAGTNLEGKAVEITTLKELKN	LEGK	AVEI	LTLKI	SLKN						
A-P/Gau	EIA	UKSGE	VIV	Elaksgevtvalndtnttqatkktgamdskt	TINT	ATKK	TGAK	IDSKT	A-P/Gau	SAGTNLEGTAVEIKTLDELKN	LEGI	AVEI	KTLDI	SLKN						
A-PKo	EIA	KSGE	VTV	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	TILL	PATKK	TGAK	DSKT	A-PKo	SAGTNLEGTAVEIKTLDELKN	LEGI	AVEI	KTLDI	SLKN						
A-IP3	EIA	KSGE	VIV	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	TINT	<b>ATKK</b>	TGAK	DSKT	A-IP3	SAGTNLEGTAVEIKTLDELKN	LEGT	AVEI	CTLD	SLKN						
A-IP90	HIS	NSGE	TI	HISNSGEITVELNDSDTTQATKKTGTWDSKT	SDTTC	ATKK	TGT	DSKT	A-IP90	SAGTNLEGKAVEITTLKELKN	LEGK	AVEI	FTLK	SLKN						
A-25015	HIS	KSGE	WIA	HISKSGEVTAELNDTDSTQATKKTGKWDAGT	TDSTC	ATKK	TGK	DAGT	A-25015	SAGTNLEGTAVEIKTLDEIKN	LEGT	AVEI	CTLD	SIKN						

'igure



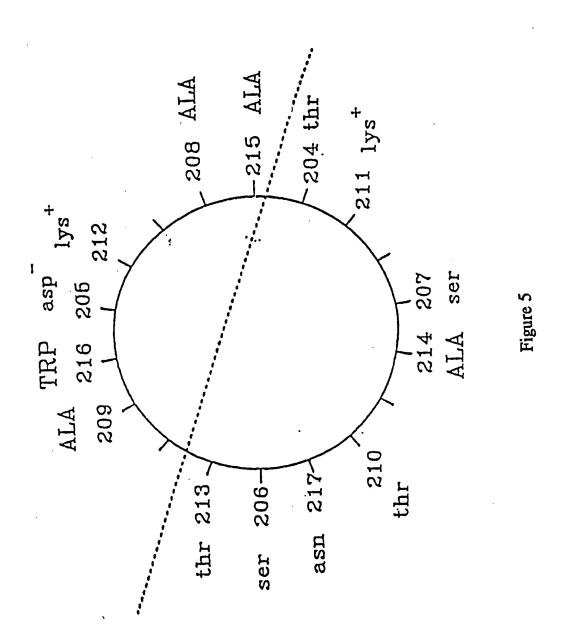
SUBSTITUTE SHEET (RULE 26)

K48: ALDDSDTTQATKKTGKWDSKT
613: ELND<u>S</u>D<u>T</u>SAATKKTAAWNSGT
625: ELNDTDSSAATKKT<u>GK</u>WNSGT
640: ELNDTDSSAATKKTAAW<u>D</u>S<u>K</u>T
613/625: ELND<u>S</u>D<u>T</u>SAATKKTGKWNSGT
613/640: ELND<u>S</u>D<u>T</u>SAATKKTAAW<u>D</u>S<u>K</u>T

ELNDTDSSAATKKTAAWNSGT

B31:

Figure 4



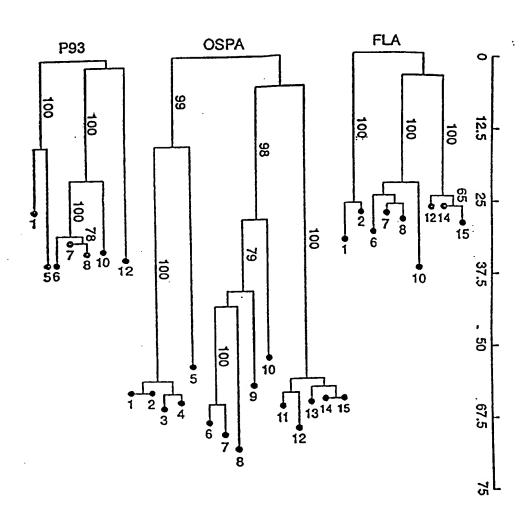


Figure 6

ATG Met 1	AAA Lys	Lys Lys	TAT Tyr	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GGT Gly	CTA Leu 10	ATA Ile	TTA Leu	GCC Ala	TTA Leu	ATA Ile 15	GCA Ala	48
TGT Cys	AAG Lys	CAA Gln	AAT Asn 20	GTT Val	AGC Ser	AGC Ser	CTT Leu	GAC Asp 25	GAG Glu	AAA Lys	AAC Asn	AGC Ser	GTT Val 30	TCA Ser	GTA Val	<b>96</b>
GAT Asp	TTG Leu	CCT Pro 35	GGT Gly	GAA Glu	ATG Met	AAA Lys	GTT Val 40	CTT Leu	GTA Val	AGC Ser	AAA Lys	GAA Glu 45	AAA Lys	AAC Asn	AAA Lys	144
			TAC Tyr													192
			GAT Asp													240
			AGT Ser													288
			GAA Glu 100													336
			TCC Ser													384
			GTA Val													432
			ACA Thr													480
_			GGC					Gly								528
-			GTT Val 180									Lys				576
			GAA Glu													624

Figure 7 (1 of 2)

		Lys											ACT Thr			672
ATT Ile 225	ACT Thr	GTA Val	AAC Asn	AGT Ser	AAA Lys 230	AAA Lys	ACT Thr	AAA Lys	GAC Asp	CTT Leu 235	GTG Val	TTT Phe	ACA Thr	AAA Lys	GAA Glu 240	720
													AAA Lys			768
													AAC Asn 270			816
AAA	TA															822

Figure 7 (2 of 2)

OSPA K48

ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala>

50 60 70 80 90

TGT AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAT AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTA TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val>

100 110 120 130 140

GAT TTA CCT GGT GGA ATG ACA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAT GGA CCA CCT TAC TGT CAA GAA CAT TCA TTT CTT TTT CTG TTT Asp Leu Pro Gly Gly Met Thr Val Leu Val Ser Lys Glu Lys Asp Lys>

150 160 170 180 190

GAC GGT AAA TAC AGT CTA GAG GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCA TTT ATG TCA GAT CTC CGT TGT CAT CTG TTC GAA CTC GAA TTT ASp Gly Lys Tyr Ser Leu Glu Ala Thr Val Asp Lys Leu Glu Leu Lys>

200 210 220 230 240

GGA ACT TCT GAT AAA AAC AAC GGT TCT GGA ACA CTT GAA GGT GAA AAA CCT TGA AGA CTA TTT TTG TTG CCA AGA CCT TGT GAA CTT CCA CTT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Thr Leu Glu Gly Glu Lys>

250 260 270 280

ACT GAC AAA AGT AAA GTA AAA TTA ACA ATT GCT GAT GAC CTA AGT CAA TGA CTG TTT TCA TTT CAT TTT AAT TGT TAA CGA CTA CTG GAT TCA GTT Thr Asp Lys Ser Lys Val Lys Leu Thr Ile Ala Asp Asp Leu Ser Gln>

290 300 310 320 330

ACT AAA TTT GAA ATT TTC AAA GAA GAT GCC AAA ACA TTA GTA TCA AAA TGA TTT AAA CTT TAA AAG TTT CTT CTA CGG TTT TGT AAT CAT AGT TTT Thr Lys Phe Glu Ile Phe Lys Glu Asp Ala Lys Thr Leu Val Ser Lys>

340 350 360 370 380

AAA GTA ACC CTT AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAC GAA TTT CAT TGG GAA TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTG CTT Lys Val Thr Leu Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

OSP A K48

400 420 430 390 AAG GGT GAA ACA TCT GAA AAA ACA ATA GTA AGA GCA AAT GGA ACC AGA TTC CCA CTT TGT AGA CTT TTT TGT TAT CAT TCT CGT TTA CCT TGG TCT Lys Gly Glu Thr Ser Glu Lys Thr Ile Val Arg Ala Asn Gly Thr Arg> 460 450 480 440 CTT GAA TAC ACA GAC ATA AAA AGC GAT GGA TCC GGA AAA GCT AAA GAA GAA CTT ATG TGT CTG TAT TTT TCG CTA CCT AGG CCT TTT CGA TTT CTT Leu Glu Tyr Thr Asp Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 510 520 500 490 GTT TTA AAA GAC TTT ACT CTT GAA GGA ACT CTA GCT GCT GAC GGC AAA CAA AAT TTT CTG AAA TGA GAA CTT CCT TGA GAT CGA CGA CTG CCG TTT Val Leu Lys Asp Phe Thr Leu Glu Gly Thr Leu Ala Ala Asp Gly Lys> 530 540 550 560 ACA ACA TTG AAA GTT ACA GAA GGC ACT GTT GTT TTA AGC AAG AAC ATT TGT TGT AAC TTT CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA Thr Thr Leu Lys Val Thr Glu Gly Thr Val Val Leu Ser Lys Asn Ile> 600 610 620 580 590 TTA AAA TCC GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT AAT TTT AGG CCT CTT TAT TGT CAA CGT GAA CTG AGA CTG TGA TGA Leu Lys Ser Gly Glu Ile Thr Val Ala Leu Asp Asp Ser Asp Thr Thr> 660 630 640 650 CAG GCT ACT AAA AAA ACT GGA AAA TGG GAT TCA AAA ACT TCC ACT TTA GTC CGA TGA TTT TTT TGA CCT TTT ACC CTA AGT TTT TGA AGG TGA AAT Gln Ala Thr Lys Lys Thr Gly Lys Trp Asp Ser Lys Thr Ser Thr Leu> 690 700 710 680 720 ACA ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA TGT TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT Thr Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys> 750 GAA GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA CTT CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT Glu Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu>

Osp A K-48

770 780 790 800 810

GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT
CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA
Glu Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala>

OSP A K48

820 TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 8 (3 of 3)

#### OSP A PGAU

	10			20	•		30			4	0		
•	•	•		•		•	•		•		•	•	
ATG AAA A	AA TAT	TTA '	TTG	GGA	ATA (	GGT (	CTA	ATA	TTA	GCC	TTA	ATA	GCA
TAC TTT T Met Lys L	TT ATA	AAT	AAC (	CUT	TAL (	CLA	ren	Tle	Leu	Ala	Leu	Ile	Alas
met Lys L	A2 IAI	Leu .	Leu	GLY		,							
50	60			7	0			80			90		
• •	•		•		•	•		•		•	•		•
TGC AAG C	TAA AAT	GTT	AGC	AGC	CTT	GAT	GAA	ብብብ፡ ጥጥጥ	AAC	AGC	CCA	TCA ACT	GTA CAT
Cys Lys G	IT TIA	CAA Val	Ser	Ser	Leu	ASD	Glu	Lvs	Asn	Ser	Ala	Ser	Val>
Cys Lys o	III V2II	VQI	561			۹۰۰۰							
100		110			120			13	0		3	40	
•.	•	•		•	•		•		•	•		•	
GAT TTG	CT GGT	GAG	ATG	AAA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	AAA TTT
CTA AAC G	GA CCA	CTC	TAC	TIT	Val	Leu	Val	Ser	Lvs	Glu	Lvs	ASD	Lvs>
ASP Leu i	TO GIY	GIU	11E C	Dy 3	***	200			_,_		_, _	p	_,
150		16	0		1	70		•	180			19	0
•	*		•	•		•		•	•		•		•
GAC GGT A	AAG TAC	AGT	CTA	AAG	GCA	ACA	GTA	CTC	AAG	ATT	CTC	CTA	AAA
CTG CCA 1	TTC ATG	TCA	CAT	TAC	Ala	Thr	Val	Asp	Lvs	Ile	Glu	Leu	Lvs>
Asp Giy	TAP IAT	261	Deu	Dys	ni.	••••			_,,				
26	00		210			22	20		2	230			240
•	•	•	•		•		•	-	~~~	-		•	•
GGA ACT	ICT GAT	AAA	GAC	AAT	GGT	TCT	CCT	CYC	CII	CAA	CCA	ACA	TTT
		TOTAL										1101	
CCT TGA	AGA CTA Ser Asd	LVS	Asp	Asn	Gly	Ser	Gly	Val	Leu	Glu	Gly	Thr	Lys>
CCT TGA	AGA CTA Ser Asp	TTT Lys	Asp	Asn	CCY	Ser	Gly	Val	Leu	Glu	Gly	Thr	Lys>
CCT TGA	AGA CTA Ser Asp 250	Lys	Asp	Asn 260	CCA	Ser	Gly 270	Val	Leu	Glu	Gly	Thr	Lys>
Gly Thr	Ser Asp 250	Lys •	Asp	Asn 260	CJÀ	Ser	Gly 270	Val	Leu	Glu ⋅ 2	Gly	Thr	
Gly Thr	Ser Asp 250 AAA AGT	Lys •	Asp GCA	Asn 260 • AAA	Gly	Ser	Gly 270	Val	Leu • GAC	Glu · 2	Gly 80 • CTA	Thr AGT	KAA
Gly Thr	Ser Asp 250 AAA AGT TTT TCA	Lys AAA TTT	Asp GCA CGT	Asn 260 AAA TTT	Gly TTA AAT	Ser ACA TGT	Gly 270 ATT TAA	Val GCT CGA	Leu GAC CTG	Glu - 2	Gly 80 CTA GAT	Thr AGT TCA	AAA
Gly Thr	Ser Asp 250 AAA AGT TTT TCA	Lys AAA TTT	Asp GCA CGT	Asn 260 AAA TTT	Gly TTA AAT	Ser ACA TGT	Gly 270 ATT TAA	Val GCT CGA	Leu GAC CTG	Glu - 2	Gly 80 CTA GAT	Thr AGT TCA	AAA
Gly Thr	Ser Asp 250 AAA AGT TTT TCA	Lys AAA TTT Lys	Asp GCA CGT	ASN 260 AAA TTT Lys	Gly TTA AAT	Ser ACA TGT	270 ATT TAA Ile	Val GCT CGA	Leu GAC CTG	Glu - 2	Gly 80 CTA GAT	AGT TCA Ser	AAA
Gly Thr : GAT GAC : CTA CTG : Asp Asp	250 AAA AGT TTT TCA Lys Ser	Lys AAA TTT Lys	GCA CGT Ala	ASN 260 AAA TTT Lys	TTA AAT Leu	ACA TGT Thr	270 ATT TAA Ile	GCT CGA Ala	GAC CTG Asp	Glu · 2: GAT CTA Asp	Gly  CTA GAT Leu  330	AGT TCA Ser	AAA TTT Lys>
Gly Thr : GAT GAC . CTA CTG . Asp Asp .	250 AAA AGT TTT TCA Lys Ser 300 TTC GAA	Lys AAA TTT Lys	GCA CGT Ala	ASN 260 AAA TTT Lys 3	TTA AAT Leu 10	ACA TGT Thr	270 ATT TAA Ile	GCT CGA Ala 320	GAC CTG ASP	Glu 2 GAT CTA Asp	Gly  CTA GAT Leu  330 GTG	AGT TCA Ser	AAA TTT Lys:
Gly Thr	250 AAA AGT TTT TCA Lys Ser 300 TTC GAA	AAA TTT Lys	GCA CGT Ala TTA AAT	ASN 260 AAA TTT Lys 3 AAA TTT	TTA AAT Leu  GAA CTT	ACA TGT Thr	Gly 270 ATT TAA Ile	GCT CGA Ala 320	GAC CTG ASP	Glu 2 GAT CTA Asp TTA AAT	Gly  BO  CTA  GAT  Leu  330  GTG  CAC	AGT TCA Ser TCA AGT	AAA TTT Lys>
Gly Thr : GAT GAC . CTA CTG . Asp Asp .	250 AAA AGT TTT TCA Lys Ser 300 TTC GAA	AAA TTT Lys	GCA CGT Ala TTA AAT	ASN 260 AAA TTT Lys 3 AAA TTT	TTA AAT Leu  GAA CTT	ACA TGT Thr	Gly 270 ATT TAA Ile	GCT CGA Ala 320 AAA TTT Lys	GAC CTG ASP ACA TGT Thr	Glu 2 GAT CTA Asp TTA AAT	Gly  BO  CTA  GAT  Leu  330  GTG  CAC	AGT TCA Ser TCA AGT Ser	AAA TTT Lys>
Gly Thr	250 AAA AGT TTT TCA Lys Ser 300 TTC GAA	AAA TTT Lys	GCA CGT Ala TTA AAT	ASN 260 AAA TTT Lys 3 AAA TTT	TTA AAT Leu  GAA CTT	ACA TGT Thr GAT CTA	Gly 270 ATT TAA Ile	GCT CGA Ala 320 AAA TTT Lys	GAC CTG ASP	Glu 2 GAT CTA Asp TTA AAT	Gly  BO  CTA  GAT  Leu  330  GTG  CAC	AGT TCA Ser TCA AGT	AAA TTT Lys>
Gly Thr	250 AAA AGT TTT TCA Lys Ser 300 TTC GAF AAG CTT Phe Glv	AAA TTT Lys GAA Leu	GCA CGT Ala TTA AAT Leu	ASN 260 AAA TTT Lys 3 AAA TTT Lys	TTA AAT Leu  10 GAA CTT Glu 360	ACA TGT Thr CTA Asp	Gly 270. ATT TAA Ile	GCT CGA Ala 320 AAA TTT Lys	GAC CTG ASP ACA TGT Thr	Glu 2 GAT CTA ASP TTA AAT Leu	Gly  CTA GAT Leu  330 GTG CAC	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> AGA TCT Arg>
Gly Thr : GAT GAC CTA CTG Asp Asp 290 ACC ACA TGG TGT Thr Thr 340 AAA GTA	Ser Asp  250  AAA AGT TTT TCA Lys Ser  300  TTC GAA AAG CTT Phe Glu  AGT TCT	AAA TTT Lys CTT GAA Leu 350	GCA CGT Ala TTA AAT Leu	ASN 260 AAA TTT Lys 3 AAA TTT Lys	TTA AAT Leu  10 GAA CTT Glu 360	ACA TGT Thr CTA Asp	ATT TAA Ile	GCT CGA Ala 320 AAA TTT Lys	GAC CTG ASP ACA TGT Thr	Glu 2 GAT CTA ASP TTA AAT Leu	Gly  CTA GAT Leu  330 CTG CAC Val	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> AGA TCT Arg>
Gly Thr	Ser Asp  250  AAA AGT TTT TCA Lys Ser  TTC GAA AAG CTT Phe Glu  AGT TCC TCA AGG	AAA TTT Lys CTT GAA Leu 350	GCA CGT Ala TTA AAT Leu GAC	ASN 260 AAA TTT Lys 3 AAA TTT Lys	TTA AAT Leu  10 GAA CTT Glu 360	ACA TGT Thr CTA Asp	Gly  2700  ATT  TAA  Ile  GGC  CCG  Gly	GCT CGA Ala 320 AAA TTT Lys 3 A GAT	GAC CTG ASP ACA TGT Thr	Glu 2 GAT CTA ASP TTA AAT Leu ATC	Gly  80  CTA GAT Leu  330  GTG CAC Val	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> AGA TCT Arg>

FIGURE 9 (1 of 3)

OSP A PGAU

410 420 400 390 AAA GGT GAA TTG TCT GCA AAA ACC ATG ACA AGA GAA AAT GGA ACC AAA TIT CCA CIT AAC AGA CGT TIT TGG TAC TGT TCT CTT TTA CCT TGG TIT Lys Gly Glu Leu Ser Ala Lys Thr Het Thr Arg Glu Asn Gly Thr Lys> 480 450 460 470 440 CTT GAA TAT ACA GAA ATG AAA AGC GAT GGA ACC GGA AAA GCT AAA GAA GAA CTT ATA TGT CTT TAC TTT TCG CTA CCT TGG CCT TTT CGA TTT CTT Leu Glu Tyr Thr Glu Met Lys Ser Asp Gly Thr Gly Lys Ala Lys Glu> 510 500 490 GTT TTA AAA AAG TTT ACT CTT GAA GGA AAA GTA GCT AAT GAT AAA GTA CAA AAT TIT TIC AAA TGA GAA CIT CCT TIT CAT CGA TIA CTA TIT CAT Val Leu Lys Lys Phe Thr Leu Glu Gly Lys Val Ala Asn Asp Lys Val> 550 560 540 ACA TTG GAA GTA AAA GAA GGA ACC GTT ACT TTA AGT AAG GAA ATT GCA TGT AAC CTT CAT TTT CTT CCT TGG CAA TGA AAT TCA TTC CTT TAA CGT Thr Leu Glu Val Lys Glu Gly Thr Val Thr Leu Ser Lys Glu Ile Ala> 600 610 590 AAA TCT GGA GAA GTA ACA GTT GCT CTT AAT GAC ACT AAC ACT ACT CAG TTT AGA CCT CTT CAT TGT CAA CGA GAA TTA CTG TGA TTG TGA TGA GTC Lys Ser Gly Glu Val Thr Val Ala Leu Asn Asp Thr Asn Thr Thr Gln> 650 660 640 GCT ACT AAA AAA ACT GGC GCA TGG GAT TCA AAA ACT TCT ACT TTA ACA CGA TGA TTT TTT TGA CCG CGT ACC CTA AGT TTT TGA AGA TGA AAT TGT Ala Thr Lys Lys Thr Gly Ala Trp Asp Ser Lys Thr Ser Thr Leu Thr> 680 ... 700 690 710 ATT AGT GTT AAC AGC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA CAA TAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT GTT Ile Ser Val Asn Ser Lys Lys Thr Thr Gln Leu Val Phe Thr Lys Gln> 760 730 750 TAC ACA ATA ACT GTA AAA CAA TAC GAC TCC GCA GGT ACC AAT TTA GAA ATG TGT TAT TGA CAT TTT GTT ATG CTG AGG CGT CCA TGG TTA AAT CTT. Tyr Thr Ile Thr Val Lys Gln Tyr Asp Ser Ala Gly Thr Asn Leu Glu>

OSP A PGAU

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820
AAA TAA
TTT ATT
Lys \*\*\*>

FIGURE 9 (3 of 3)

ATG Met 1	AAA Lys	AAA Lys	TAT Tyr	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GGT Gly	CTA Leu 10	ATA Ile	TTA Leu	GCT Ala	TTA Leu	ATA Ile 15	GCA Ala	48
TGT Cys	AAG Lys	CAA Gln	AAT Asn 20	GTT Val	AGC Ser	AGC Ser	CTT Leu	GAC Asp 25	GAG Glu	AAA Lys	AAC Asn	AGC Ser	GTT Val 30	TCA Ser	GTA Val	96
GAT Asp	TTG Leu	CCT Pro 35	GGT Gly	GAA Glu	ATG Met	AAA Lys	GTT Val 40	CTT Leu	GTA Val	AGC Ser	AAA Lys	GAA Glu 45	AAA Lys	GAC Asp	AAA Lys	144
GAC Asp	GGC Gly 50	AAG Lys	TAC Tyr	AGT Ser	CTA Leu	ATG Met 55	GCA Ala	ACA Thr	GTA Val	GAC Asp	AAG Lys 60	CTT Leu	GAG Glu	CTT Leu	AAA Lys	192

#### 16/133 🔎

GGA Gly 65	ACA Thr	TCT Ser	GAT Asp	AAA Lys	AAC Asn 70	AAT Asn	GGA Gly	TCT Ser	GGG Gly	GTG Val 75	CTT Leu	GAA Glu	GGC Gly	GTA Val	AAA Lys 80	240
GCT Ala	GAC Asp	AAA Lys	AGC Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	GTT Val 90	TCT Ser	GAC Asp	GAT Asp	CTÀ Leu	AGC Ser 95	ACA Thr	288
ACC Thr	ACA Thr	CTT Leu	GAA Glu 100	GTT Val	TTA Leu	AAA Lys	GAA Glu	GAT Asp 105	GGC Gly	AAA Lyb	ACA Thr	TTA Leu	GTG Val 110	TCA Ser	AAA Lys	336
AAA Lys	AGA Arg	ACT Thr 115	TCT Ser	AAA Lys	GAT Așp	AAG Lys	TCA Ser 120	TCA Ser	ACA Thr	GAA Glu	GAA Glu	AAG Lys 125	TTC Phe	AAT Asn	GAA Glu	384
AAA Lys	GGC Gly 130	Glu	TTA Leu	GTT Val	GAA Glu	AAA Lys 135	Ile	ATG Met	GCA Ala	AGA Arg	GCA Ala 140	No.	GGA Gly	ACC Thr	ATA Ile	432
CTT Leu 145	Glu	TAC Tyr	ACA Thr	GGA Gly	ATT Ile 150	. Lys	AGC Ser	GAT Asp	GGA Gly	TCC Ser 155	GGA Gly	AAA Lys	GCT Ala	AAA Lys	GAA Glu 160	480
ACT Thr	TTA Leu	AAA Lys	GAA Glu	TAT Tyr 165	Val	CTT Leu	GAA Glu	GGA Gly	ACT Thr 170	Leu	ACT Thr	GCT Ala	GAA Glu	AAA Lys 175	GCA Ala	528
ACA Thr	TTG	GTG Val	GTT Val 180	Lys	GAA Glu	GGA Gly	ACT Thr	GTT Val 185	The	TTA Leu	AGT Ser	AAG	CAC His 190		TCA Ser	576
AAA Lys	TCT Ser	GGA Gly 195	Glu	GTA Val	ACA Thr	GCT	GAA Glu 200	Leu	TAA : naA :	GAC Asp	ACT Thr	GAC Asp 205	Jer	ACI Thr	CAA Gln	624
GCI Ala	ACT Thr 210	Lys	AAA Lys	ACI Thr	GGG Gly	Lys 215	Tr	GAI Asp	GCA Ala	GGC Gly	ACT Thr 220	Ser	ACT Thr	TT?	ACA Thr	672
AT1 116 225	?Thr	GT?	AAC L Asr	AAC Asr	230	. Ly	A ACI	Lys	A GCC	CTT a Lev 235	ı va.	A TTT	r ACA e Thr	AAI Lys	CAA Gln 240	720
GA(	ACI Thi	ATT	Thi	TCI Sei 24!	Gl	A AAI n Ly:	A TAC	C Asi	C TCI P Sei 250	L WIS	A GGI	A ACC	C AAC	25!	G GAA 1 Glu 5	768
GG( Gl)	C ACI	A GC	A GTG a Va: 260	l GJ	A AT	r aa e Ly	A AC	A CT r Let 26	u As	r GAI p Gl	A CT	T AAI	A AAG B ASI 270		r TTA a Leu	816
AG Ar																. 819

Figure 10 (2 of 2)

430

420

OSP B B-31 Sequence Range: 1 to 891

30 20 10 ATG AGA TTA TTA ATA GGA TTT GCT TTA GCG TTA GCT TTA ATA GGA TGT TAC TOT AAT AAT TAT COT AAA CGA AAT CGC AAT CGA AAT TAT COT ACA Met Arg Leu Leu Ile Gly Phe Ala Leu Ala Leu Ile Gly Cys> 90 80 70 60 • GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT Ala Glm Lys Gly Ala Glu Ser Ile Gly Ser Glm Lys Glu Asm Asp Leu> 130 120 110 100 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG Asn Leu Glu Asp Ser Ser Lys Lys Ser His Gln Asn Ala Lys Gln Asp> 150 170 160 150 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT Leu Pro Ala Val Thr Glu Asp Ser Val Ser Leu Phe Asm Gly Asm Lys> 240 230 220 200 210 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT Ile Phe Val Ser Lys Glu Lys Asn Ser Ser Gly Lys Tyr Asp Leu Arg> 260 270 250 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA Ala Thr Ile Asp Gln Val Glu Leu Lys Gly Thr Ser Asp Lys Asn Asn> 310 320 300 290 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT Gly Ser Gly Thr Leu Glu Gly Ser Lys Pro Asp Lys Ser Lys Val Lys> 370 360 350 340 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA Leu Thr Val Ser Ala Asp Leu Asn Thr Val Thr Leu Glu Ala Phe Asp>

410

400

390

GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT Ala Ser Asn Gln Lys Ile Ser Ser Lys Val Thr Lys Lys Gln Gly Ser> 470 460 450 ATA ACA GAG GAA ACT CTC AAA GCT AAT AAA TTA GAC TCA AAG AAA TTA TAT TGT CTC CTT TGA GAG TTT CGA TTA TTT AAT CTG AGT TTC TTT AAT Ile Thr Glu Glu Thr Leu Lys Ala Asn Lys Leu Asp Ser Lys Lys Leu> 500 510 490 ·**\_**• ACA AGA TCA AAC GGA ACT ACA CTT GAA TAC TCA CAA ATA ACA GAT GCT TGT TCT AGT TTG CCT TGA TGT GAA CTT ATG AGT GTT TAT TGT CTA CGA Thr Arg Ser Asn Gly Thr Thr Leu Glu Tyr Ser Gln Ile Thr Asp Ala> 570 560 550 540 530 GAC AAT GCT ACA AAA GCA GTA GAA ACT CTA AAA AAT AGC ATT AAG CTT CTG TTA CGA TGT TTT CGT CAT CTT TGA GAT TTT TTA TCG TAA TTC GAA Asp Asn Ala Thr Lys Ala Val Glu Thr Leu Lys Asn Ser Ile Lys Leu> 600 590 580 GAA GGA AGT CTT GTA GTC GGA AAA ACA ACA GTG GAA ATT AAA GAA GGT CTT CCT TCA GAA CAT CAG CCT TTT TGT TGT CAC CTT TAA TTT CTT CCA Glu Gly Ser Leu Val Val Gly Lys Thr Thr Val Glu Ile Lys Gl: Gly> 650 660 640 630 ACT GTT ACT CTA AAA AGA GAA ATT GAA AAA GAT GGA AAA GTA AAA GTC TGA CAA TGA GAT TTT TCT CTT TAA CTT TTT CTA CCT TTT CAC TTT CAG Thr Val Thr Leu Lys Arg Glu Ile Glu Lys Asp Gly Lys Val Lys Val> 700 710 690 680 TTT TTG AAT GAC ACT GCA GGT TCT AAC AAA AAA ACA GGT AAA TGG GAA AAA AAC TTA CTG TGA CGT CCA AGA TTG TTT TTT TGT CCA TTT ACC CTT Phe Leu Asn Asp Thr Ala Gly Ser Asn Lys Lys Thr Gly Lys Trp Glu> 750 740 730 GAC AGT ACT AGC ACT TTA ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA CTG TCA TGA TCG TGA AAT TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT Asp Ser Thr Ser Thr Leu Thr Ile Ser Ala Asp Ser Lys Lys Thr Lys> 800 810 790 780 GAT TTG GTG TTC TTA ACA GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC CTA AAC CAC AAG AAT TGT CTA CCA TGT TAA TGT CAT GTT ATG TTG Asp Leu Val Phe Leu Thr Asp Gly Thr Ile Thr Val Gln Gln Tyr Asn>

820 830 840 850 860

ACA GCT GGA ACC AGC CTA GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TGT CGA CCT TGG TCG GAT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA Thr Ala Gly Thr Ser Leu Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu>

870 880 890

TCA GAG CTT AAA AAC GCT TTA AAA TAA AGT CTC GAA TTT TTG CGA AAT TTT ATT Ser Glu Leu Lys Asn Ala Leu Lys \*\*\*>

OspC-B31 Sequence Range: 1 to 633

10 20 30 40

ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TTA TTT TTC TTA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA MET Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe>

50 60 70 80 90

ATA TCT TGT AAT AAT TCA GGG AAA GAT GGG AAT ACA TCT GCA AAT TCT TAT AGA ACA TTA TTA AGT CCC TTT CTA CCC TTA TGT AGA CGT TTA AGA Ile Ser Cys Asn Asn Ser Gly Lys Asp Gly Asn Thr Ser Ala Asn Ser>

100 110 120 130 140

GCT GAT GAG TCT GTT AAA GGG CCT AAT CTT ACA GAA ATA AGT AAA AAA CGA CTA CTC AGA CAA TTT CCC GGA TTA GAA TGT CTT TAT TCA TTT TTT Ala Asp Glu Ser Val Lys Gly Pro Asn Leu Thr Glu Ile Ser Lys Lys>

150 160 170 180 190

ATT ACG GAT TCT AAT GCG GTT TTA CTT GCT GTG AAA GAG GTT GAA GCG TAA TGC CTA AGA TTA CGC CAA AAT GAA CGA CAC TTT CTC CAA CTT CGC Ile Thr Asp Ser Asn Ala Val Leu Leu Ala Val Lys Glu Val Glu Ala>

200 210 220 230 240

TTG CTG TCA TCT ATA GAT GAA ATT GCT GCT AAA GCT ATT GGT AAA AAA AAC GAC AGT AGA TAT CTA CTT TAA CGA CGA TTT CGA TAA CCA TTT TTT Leu Leu Ser Ser Ile Asp Glu Ile Ala Ala Lys Ala Ile Gly Lys Lys>

250 260 270 280

ATA CAC CAA AAT AAT GGT TTG GAT ACC GAA TAT AAT CAC AAT GGA TCA TAT GTG GTT TTA TTA CCA AAC CTA TGG CTT ATA TTA GTG TTA CCT AGT Ile His Gln Asn Asn Gly Leu Asp Thr Glu Tyr Asn His Asn Gly Ser>

290 300 310 320 330

TTG TTA GCG GGA CGT TAT GCA ATA TCA ACC CTA ATA AAA CAA AAA TTA AAC AAT CGC CCT GCA ATA CGT TAT AGT TGG GAT TAT TTT GTT TTT AAT Leu Leu Ala Gly Arg Tyr Ala Ile Ser Thr Leu Ile Lys Gln Lys Leu>

340 350 360 370 380

OspC-B31

430 420 400 390 ARA TGT TCT GAR ACA ITT ACT ART ARA TTR ARA GAR ARA CAC ACA GAT TIT ACA AGA CIT TGT AAA TGA TTA TIT AAT TIT CIT TIT GTG TGT CTA Lys Cys Ser Glu Thr Phe Thr Asn Lys Leu Lys Glu Lys His Thr Asp> 450 CTT GGT AAA GAA GGT GTT ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA GAA CCA TTT CTT CCA CAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT Leu Gly Lys Glu Gly Val Thr Asp Ala Asp Ala Lys Glu Ala Ile Leu> 510 --- . 500 490 AAA ACA AAT GGT ACT AAA ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TIT TGT TTA CCA TGA TTT TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT Lys Thr Asn Gly Thr Lys Thr Lys Gly Ala Glu Glu Leu Gly Lys Leu> 570 550 560 540 530 TTT GAA TCA GTA GAG GTC TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAA CTT AGT CAT CTC CAG AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA Phe Glu Ser Val Glu Val Leu Ser Lys Ala Ala Lys Glu Met Leu Ala> 620 610 600 580 590 AAT TCA GTT AAA GAG CTT ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA TTA AGT CAA TTT CTC GAA TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser Pro Lys> 630 AAA CCT TAA TTT GGA ATT Lys Pro \*\*\*>

FIGURE 12 (2 of 2)

PCT/US94/12352

OspC-K48 Sequence Range: 1 to 630 22/133

		. 1	LO	•		20			30			•	40 .		
> m~	•		* >>T	202	mer a	• •		• •	44.y	NTC	ACT	TT A	4444	444.	~~~
															AAA
															Phe>
	, -														
50			60			•	70			80			90		
♣.		•	•		•		•	•		•		•	•		•
			-								TCT				
											AGA				
116	Ser	cys	ASII	ASII	Ser	GIÅ	GIA	ASP	Thr	Vīg.	Ser	Inr	ASN	Pro	Asp>
10	00		1	110			120			13	30		:	140	
	•	•		•		•	•		•		•	•		•	
GAG	TCT	GCA	AAA	GGA	CCT	TAA	CTT	ACA	GTA	ATA	AGC	AAA	AAA	ATT	ACA
											TCG				
Glu	Ser	Ala	Lys	Gly	Pro	Asn	Leu	Thr	Val	lle	Ser	Lys	Lys	Ile	Thr>
-	150			1 /	50		7	170			180			1 (	90
•	*	,	•		•	*	-	*		•	•		•	1,3	*
GAT	TCT	AAT	GCA	TTT	GTA	CTG	GCT	GTG	AAA	GAA	GTT	GAG	GCT	TTG	ATC
CTA	AGA	TTA	CGT	AAA	CAT	GAC	CGA	CAC	TTT	CTT	CAA	CTC	CGA	AAC	TAG
Asp	Ser	Asn	Ala	Phe	Val	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala	Leu	Ile>
	:	200			210			22	20		2	230			240
•	:	200		•	210		•	22	20	•	2	230		•	240
	TCT	* ATA			CTT			ААА	• GCT		GGT	·• AAA			• CAT
AGT	TCT AGA	ATA TAT	CTA	CTT	CTT GAA	CGA	TTA	AAA TTT	• GCT CGA	TAA	GGT CCA	AAA TTT	CAT	TAT	CAT GTA
AGT	TCT AGA	ATA TAT	CTA	CTT	CTT GAA	CGA	TTA	AAA TTT	• GCT CGA	TAA	GGT CCA	AAA TTT	CAT	TAT	CAT
AGT	TCT AGA	ATA TAT Ile	CTA	CTT	CTT GAA Leu	CGA	TTA	AAA TTT	• GCT CGA	TAA	GGT CCA	AAA TTT	CAT Val	TAT	CAT GTA
AGT Ser	TCT AGA Ser	ATA TAT Ile	CTA Asp	CTT Glu	CTT GAA Leu	CGA Ala 260	TTA Asn	AAA TTT Lys	GCT CGA Ala 270	TAA Ile	GGT CCA Gly	AAA TTT Lys	CAT Val	TAT Ile	CAT GTA His>
AGT Ser CAA	TCT AGA Ser	ATA TAT Ile 2:	CTA Asp 50 GGT	CTT Glu • TTA	CTT GAA Leu	CGA Ala 260 GCT	TTA Asn AAT	AAA TTT Lys • GCG	GCT CGA Ala 270 GGT	TAA Ile CAA	GGT CCA Gly	AAA TTT Lys 28 GGA	CAT Val 30 TCA	TAT Ile	CAT GTA His>
AGT Ser CAA GTT	TCT AGA Ser • AAT	ATA TAT Ile 2: AAT TTA	CTA Asp  60 GGT CCA	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA	TTA Asn AAT TTA	AAA TTT Lys GCG CGC	GCT CGA Ala 270 GGT CCA	TAA Ile CAA GTT	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 30 TCA AGT	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT	TCT AGA Ser • AAT	ATA TAT Ile 2: AAT TTA	CTA Asp  60 GGT CCA	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA	TTA Asn AAT TTA	AAA TTT Lys GCG CGC	GCT CGA Ala 270 GGT CCA	TAA Ile CAA GTT	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 30 TCA AGT	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT	TCT AGA Ser • AAT	ATA TAT Ile 2: AAT TTA	CTA Asp  60 GGT CCA	CTT Glu TTA AAT	CTT GAA Leu AAT TTA	CGA Ala 260 GCT CGA Ala	TTA Asn AAT TTA	AAA TTT Lys GCG CGC	GCT CGA Ala 270 GGT CCA Gly	TAA Ile CAA GTT	GGT CCA Gly AAC TTG	AAA TTT Lys 28 GGA CCT	CAT Val 30 TCA AGT	TAT Ile TTG AAC	CAT GTA His>
AGT Ser CAA GTT Gln 290	TCT AGA Ser * AAT TTA Asn	ATA TAT Ile 2: AAT TTA Asn	CTA Asp 50 GGT CCA Gly 300	CTT Glu TTA AAT Leu	CTT GAA Leu AAT TTA Asn	CGA Ala 260 GCT CGA Ala	TTA ASD AAT TTA ASD	AAA TTT Lys GCG CGC Ala	GCT CGA Ala 270 GGT CCA Gly	CAA GTT Gln	GGT CCA Gly * AAC TTG Asn	AAA TTT Lys 28 GGA CCT Gly	CAT Val 30 TCA AGT Ser 330	TAT Ile TTG AAC Leu	CAT GTA His>
AGT Ser CAA GTT Gln 290	TCT AGA Ser AAT TTA Asn	ATA TAT Ile 2: AAT TTA Asn	CTA Asp 50 GGT CCA Gly 300 TAT	CTT Glu TTA AAT Leu	CTT GAA Leu AAT TTA Asn	CGA Ala 260 GCT CGA Ala 31	AAT TTA ASD	AAA TTT Lys GCG CGC Ala	GCT CGA Ala 270 GGT CCA Gly	CAA GTT Gln	GGT CCA Gly AAC TTG Asn	AAA TTT Lys 28 GGA CCT Gly	CAT Val 30 TCA AGT Ser 330	TAT Ile TTG AAC Leu	CAT GTA His> TTA AAT Leu>
CAA GTT Gln 290 GCA CGT	TCT AGA Ser AAT TTA ASD	ATA TAT Ile 2: AAT TTA ASD	CTA Asp 50 GGT CCA Gly 300 TAT ATA	CTT Glu TTA AAT Leu GCA CGT	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA AGT	AAT TTA ASN  10 ACC TGG	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 * ACA TGT	GGT CCA Gly AAC TTG ASD GAA CTT	AAA TTT Lys 28 GGA CCT Gly	CAT Val 30 TCA AGT Ser 330 TTA AAT	TAT Ile TTG AAC Leu AGT TCA	CAT GTA His> TTA AAT Leu> AAA TTT
CAA GTT Gln 290 GCA CGT	TCT AGA Ser AAT TTA ASD	ATA TAT Ile 2: AAT TTA ASD	CTA Asp 50 GGT CCA Gly 300 TAT ATA	CTT Glu TTA AAT Leu GCA CGT	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA AGT	AAT TTA ASN  10 ACC TGG	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 * ACA TGT	GGT CCA Gly AAC TTG ASD GAA CTT	AAA TTT Lys 28 GGA CCT Gly	CAT Val 30 TCA AGT Ser 330 TTA AAT	TAT Ile TTG AAC Leu AGT TCA	CAT GTA His> TTA AAT Leu>
CAA GTT Gln 290 GCA CGT Ala	TCT AGA Ser AAT TTA ASD	ATA TAT Ile 2: AAT TTA ASD	CTA ASP SO GGT CCA Gly 300 TAT ATA Tyr	CTT Glu TTA AAT Leu GCA CGT	CTT GAA Leu AAT TTA ASD	CGA Ala 260 GCT CGA Ala 3: TCA AGT	AAT TTA ASN  10 ACC TGG	AAA TTT Lys GCG CGC Ala CTA GAT	GCT CGA Ala 270 GGT CCA Gly ATA TAT	CAA GTT Gln 320 ACA TGT	GGT CCA Gly AAC TTG ASD GAA CTT	AAA TTT Lys 28 GGA CCT Gly	CAT Val 30 TCA AGT Ser 330 TTA AAT Leu	TAT Ile TTG AAC Leu AGT TCA	CAT GTA His> TTA AAT Leu> AAA TTT
CAA GTT Gln 290 • GCA CGT Ala	TCT AGA Ser AAT TTA Asn CCT Gly	ATA TAT Ile 2: AAT TTA Asn GCC CGG Ala	CTA ASP 50 GGT CCA Gly 300 TAT ATA Tyr	TTA AAT Leu  GCA CGT Ala 350	CTT GAA Leu AAT TTA Asn ATA TAT Ile	CGA Ala 260 GCT CGA Ala 3: TCA AGT Ser	AAT TTA ASN 10 ACC TGG Thr 360	AAA TTT Lys GCG CGC Ala CTA GAT Leu	GCT CGA Ala 270 GGT CCA Gly ATA TAT Ile	CAA GTT Gln 320 ACA TGT Thr	GGT CCA Gly AAC TTG Asn GAA CTT Glu	AAA TTT Lys  28 GGA CCT Gly  AAA TTT Lys	CAT Val 30 TCA AGT Ser 330 TTA AAT Leu	TAT Ile TTG AAC Leu AGT TCA Ser	CAT GTA His>  TTA AAT Leu>  AAA TTT Lys>
CAA GTT Gln 290 GCA CGT Ala 3	TCT AGA Ser AAT TTA Asn CCT Gly	ATA TAT Ile 2: AAT TTA Asn GCC CGG Ala	CTA ASP 50 GGT CCA Gly 300 TAT ATA Tyr	CTT Glu TTA AAT Leu GCA CGT Ala	CTT GAA Leu AAT TTA ASD ATA TAT Ile	CGA Ala 260 GCT CGA Ala 3: TCA AGT Ser	AAT TTA ASN 10 ACC TGG Thr 360 AAT	AAA TTT Lys GCG CGC Ala CTA GAT Leu	GCT CGA Ala 270 GGT CCA Gly ATA TAT Ile	CAA GTT Gln 320 ACA TGT Thr	GGT CCA Gly AAC TTG Asn GAA CTT Glu	AAA TTT Lys  28 GGA CCT Gly  AAA TTT Lys	CAT Val 30 TCA AGT Ser 330 TTA AAT Leu	TAT Ile TTG AAC Leu AGT TCA Ser	CAT GTA His>  TTA AAT Leu>  AAA TTT Lys>
CAA GTT Gln 290 GCA CGT Ala 3	TCT AGA Ser AAT TTA Asn CCT Gly 40 . AAA TTT	ATA TAT Ile 2: AAT TTA Asn * GCC CGG Ala AAT TTA	CTA ASP 50 CGT CCA Gly 300 TAT ATA Tyr TCA AGT	CTT Glu TTA AAT Leu GCA CGT Ala 350	CTT GAA Leu AAT TTA ASD ATA TAT Ile GAG CTC	CGA Ala 260 GCT CGA Ala 3: TCA AGT Ser	AAT TTA ASN  ACC TGG Thr  360 AAT TTA	AAA TTT Lys GCG CGC Ala CTA GAT Leu	GCT CGA Ala 270 GGT CCA Gly ATA TAT Ile	CAA GTT Gln 320 ACA TGT Thr	GGT CCA Gly AAC TTG ASD GAA CTT Glu	AAA TTT Lys  GGA CCT Gly  AAA TTT Lys  GAG CTC	CAT Val 30 TCA AGT Ser 330 TTA AAT Leu	TAT Ile TTG AAC Leu AGT TCA Ser	CAT GTA His>  TTA AAT Leu>  AAA TTT Lys>

OspC-K48

410 420 400 390 CAT TCT GAA GCA TTT ACT AAT AGA CTA AAA GGT TCT CAT GCA CAA CTT GTA AGA CTT CGT AAA TGA TTA TCT GAT TTT CCA AGA GTA CGT GTT GAA His Ser Glu Ala Phe Thr Asn Arg Leu Lys Gly Ser His Ala Gln Leu> 460 470 480 440 GGA GTT GCT GCT ACT GAT GAT CAT GCA AAA GAA GCT ATT TTA AAG CCT CAA CGA CGA CGA TGA CTA CTA GTA CGT TTT CTT CGA TAA AAT TTC Gly Val Ala Ala Ala Thr Asp Asp His Ala Lys Glu Ala Ile Leu Lys> 490 500 510 520 TCA AAT CCT ACT AAA GAT AAG GGT GCT AAA GCA CTT AAA GAC TTA TCT AGT TTA GGA TGA TTT CTA TTC CCA CGA TTT CGT GAA TTT CTG AAT AGA Ser Asn Pro Thr Lys Asp Lys Gly Ala Lys Ala Leu Lys Asp Leu Ser> 550 560 570 530 540 GAA TCA GTA GAA AGC TTG GCA AAA GCA GCG CAA GAA GCA TTA GCT AAT CTT AGT CAT CTT TCG AAC CGT TTT CGT CGC GTT CTT CGT AAT CGA TTA Glu Ser Val Glu Ser Leu Ala Lys Ala Ala Gln Glu Ala Leu Ala Asn> 580 590 600 610 620 TCA GTT AAA GAA CTT ACA AAT CCT GTT GTG GCA GAA AGT CCA AAA AAA AGT CAA TIT CIT GAA TGT TIA GGA CAA CAC CGT CIT TCA GGT TIT TIT Ser Val Lys Glu Leu Thr Asn Pro Val Val Ala Glu Ser Pro Lys Lys> CCT TAA GGA ATT Pro \*\*\*>

FIGURE 13 (2 of 2)

PCT/US94/12352

24/133

OspC-PKO Sequence Range: 1 to 639

30 40 20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TTT TTC TTA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 70 80 90 60 50 ATA TCT TGT AGT AAT TCA GGG AAA GGT GGG GAT TCT GCA TCT ACT AAT TAT AGA ACA TCA TTA AGT CCC TTT CCA CCC CTA AGA CGT AGA TGA TTA Ile Ser Cys Ser Asn Ser Gly Lys Gly Gly Asp Ser Ala Ser Thr Asn> 110 120 CCT GCT GAC GAG TCT GCG AAA GGG CCT AAT CTT ACA GAA ATA AGC AAA GGA CGA CTG CTC AGA CGC TTT CCC GGA TTA GAA TGT CTT TAT TCG TTT Pro Ala Asp Glu Ser Ala Lys Gly Pro Asn Leu Thr Glu Ile Ser Lys> 170 160 180 AAA ATT ACA GAT TCT AAT GCA TTT GTA CTT GCT GTT AAA GAA GTT GAG TTT TAA TGT CTA AGA TTA CGT AAA CAT GAA CGA CAA TTT CTT CAA CTC Lys Ile Thr Asp Ser Asn Ala Phe Val Leu Ala Val Lys Glu Val Glu> 220 230 240 200 210 ACT TTG GTT TTA TCT ATA GAT GAA CTT GCT AAG AAA GCT ATT GGT CAA TGA AAC CAA AAT AGA TAT CTA CTT GAA CGA TTC TTT CGA TAA CCA GTT Thr Leu Val Leu Ser Ile Asp Glu Leu Ala Lys Lys Ala Ile Gly Gln> 260 270 280 250 AAA ATA GAC AAT AAT AAT GGT TTA GCT GCT TTA AAT AAT CAG AAT GGA TTT TAT CTG TTA TTA TTA CCA AAT CGA CGA AAT TTA TTA GTC TTA CCT Lys Ile Asp Asn Asn Asn Gly Leu Ala Ala Leu Asn Asn Gln Asn Gly> 290 300 310 320 330 TCG TTG TTA GCA GGA GCC TAT GCA ATA TCA ACC CTA ATA ACA GAA AAA AGC AAC AAT CGT CCT CGG ATA CGT TAT AGT TGG GAT TAT TGT CTT TTT Ser Leu Leu Ala Gly Ala Tyr Ala Ile Ser Thr Leu Ile Thr Glu Lys> 340 350 360 370 380 TTG AGT AAA TTG AAA AAT TTA GAA GAA TTA AAG ACA GAA ATT GCA AAG AAC TCA TTT AAC TTT TTA AAT CTT CTT AAT TTC TGT CTT TAA CGT TTC Leu Ser Lys Leu Lys Asn Leu Glu Glu Leu Lys Thr Glu Ile Ala Lys>

OspC-PKO

Pro Lys Lys Pro \*\*\*>

420 410 400 390 GCT AAG AAA TGT TCC GAA GAA TTT ACT AAT AAA CTA AAA AGT GGT CAT CGA TTC TTT ACA AGG CTT CTT AAA TGA TTA TTT GAT TTT TCA CCA GTA Ala Lys Lys Cys Ser Glu Glu Phe Thr Asn Lys Leu Lys Ser Gly His> 470 450 440 GCA GAT CTT GGC AAA CAG GAT GCT ACC GAT GAT CAT GCA AAA GCA GCT CGT CTA GAA CCG TTT GTC CTA CGA TGG CTA CTA GTA CGT TTT CGT CGA Ala Asp Leu Gly Lys Gln Asp Ala Thr Asp Asp His Ala Lys Ala Ala> 520 490 500 ATT TTA AAA ACA CAT GCA ACT ACC GAT AAA GGT GCT AAA GAA TTT AAA TAA AAT TIT TGT GTA CGT TGA TGG CTA TIT CCA CGA TIT CTT AAA TIT Ile Leu Lys Thr His Ala Thr Thr Asp Lys Gly Ala Lys Glu Phe Lys> 560 570 550 540 530 GAT TTA TTT GAA TCA GTA GAA GGT TTG TTA AAA GCA GCT CAA GTA GCA CTA AAT AAA CTT AGT CAT CTT CCA AAC AAT TTT CGT CGA GTT CAT CGT Asp Leu Phe Glu Ser Val Glu Gly Leu Leu Lys Ala Ala Gln Val Ala> 610 620 600 590 580 CTA ACT AAT TCA GTT AAA GAA CTT ACA AGT CCT GTT GTA GCA GAA AGT GAT TGA TTA AGT CAA TTT CTT GAA TGT TCA GGA CAA CAT CGT CTT TCA Leu Thr Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser> 630 CCA AAA AAA CCT TAA GGT TTT TTT GGA ATT

FIGURE 14 (2 of 2)

OspC-TRO Sequence Range: 1 to 624

10 20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TIT TIC TIA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 70 80 60 50 ATA TCT TGT AAT AAT TCA GGT GGG GAT TCT GCA TCT ACT AAT CCT GAT TAT AGA ACA TTA TTA AGT CCA CCC CTA AGA CGT AGA TGA TTA GGA CTA Ile Ser Cys Asn Asn Ser Gly Gly Asp Ser Ala Ser Thr Asn Pro Asp> 130 140 110 100 GAG TCT GCA AAA GGA CCT AAT CTT ACC GTA ATA AGC AAA AAA ATT ACA CTC AGA CGT TTT CCT GGA TTA GAA TGG CAT TAT TCG TTT TTT TAA TGT Glu Ser Ala Lys Gly Pro Asn Leu Thr Val Ile Ser Lys Lys Ile Thr> 160 180 150 GAT TCT AAT GCA TTT TTA CTG GCT GTG AAA GAA GTT GAG GCT TTG CTT CTA AGA TTA CGT AAA AAT GAC CGA CAC TTT CTT CAA CTC CGA AAC GAA Asp Ser Asn Ala Phe Leu Leu Ala Val Lys Glu Val Glu Ala Leu Leu> 220 230 .240 210 TCA TCT ATA GAT GAA CTT TCT AAA GCT ATT GGT AAA AAA ATA AAA AAT AGT AGA TAT CTA CTT GAA AGA TTT CGA TAA CCA TTT TTT TAT TTT TTA Ser Ser Ile Asp Glu Leu Ser Lys Ala Ile Gly Lys Lys Ile Lys Asn> 270 250 260 GAT GGT ACT TTA GAT AAC GAA GCA AAT CGA AAC GAA TCA TTG ATA GCA CTA CCA TGA AAT CTA TTG CTT CGT TTA GCT TTG CTT AGT AAC TAT CGT Asp Gly Thr Leu Asp Asn Glu Ala Asn Arg Asn Glu Ser Leu Ile Ala> 290 300 310 320 330 GGA GCT TAT GAA ATA TCA AAA CTA ATA ACA CAA AAA TTA AGT GTA TTG CCT CGA ATA CTT TAT AGT TTT GAT TAT TGT GTT TTT AAT TCA CAT AAC Gly Ala Tyr Glu Ile Ser Lys Leu Ile Thr Gln Lys Leu Ser Val Leu> 370 350 360 380 AAT TCA GAA GAA TTA AAG AAA AAA ATT AAA GAG GCT AAG GAT TGT TCC TTA AGT CTT CTT AAT TTC TTT TTA TTT CTC CGA TTC CTA ACA AGG

Asn Ser Glu Glu Leu Lys Lys Lys Ile Lys Glu Ala Lys Asp Cys Ser>

OSDC-TRO

390			40	0		4	10			420			43	0
391	,	•		•	•		•		•	•		•		•
GAA AA		» CT	л <i>~</i> т	N N G	СТА	AAA	GAT	AGT	CAT	GCA	GAG	CTT	GGT	ATA
CTT TT	4 111	WC1	WC1	MATC.	CAT	J-J-J	CTA	TCA	GTA	CGT	CTC	GAA	CCA	TAT
CTT TT	AAA 1	TGA	TGA	110	tan	tuc	yen	Car	His	Ala	Glu	Leu	Glv	Ile>
Glu Ly	s Phe	Thr	Thr	Lys	Leu	ւրչ	vah	JC1						
				450			46	in.		4	170			480
	440			450			•	*	•		•		•	•
•	•		•						~~m	) TYT	energy.		»C»	ርእጥ
CAA AG	C GTT	CAG	GAT	GAT	AAT	GCA	AAA	AAA	GC1	WII	117	~~~	W-W	CTA
GTT TC	G CAA	GTC	CTA	CTA	TTA	CGT	TTT	1-1-I.	CGA	TAA	AAT.	TIT	101	GIA
Gln Se	r Val	Gln	Asp	Asp	Asn	Ala	Lys	Lys	Ala	Ile	Leu	Lys	Thr	H72>
_										~ .,				
	4	90			500			510			5	20		•
•		*	*		•		•	•		•		•	•	
GGA AC	T AAZ	GAC	AAG	GGT	GCT	AAA	GAA	CTT	GAA	GAG	TTA	TTT	AAA	TCA
	- mm	· CTC	بعب	CCA	CGA	TTT	CTT	GAA	CTT	CTC	AAT	AAA	1-1-1	AGT
Gly Th	r Tay	. Asn	Lvs	Gly	Ala	Lys	Glu	Leu	Glu	Glu	Leu	Phe	Lys	Ser>
Gly II	ı wy.	,	-2 -	•		-						•		
530		540			5	50			560			570		
	•			•		*	•		•		•	. •		•
CTA G	A AC	~ <b>ग</b> गर	: ጥርል	AAA	GCA	GCG	CAA	GCA	GCA	TTA	ACT	TAA	TCA	GTT
GAT C	W TC	~ 330	ACT	Label	CGT	CGC	GTT	CGT	CGI	' AAT	TGA	ATT	AGT	CAA
Leu G	1 1C	- In	Cor	TVS	Ala:	Ala	Gln	Ala	Ala	Leu	Thr	Asn	Ser	Val>
Leu G.	u se	. Lec	Ser	<i></i>										
500			590			600	)		6	10			620	
580		_	) <del> </del>		•	•				4	•		•	
AAA G		- - \01			י כייי	CTC	: CCA	GAR	AGT	r cca	AAA	AAA	CCI	TAA
AAA G. TTT C	AG CT	T AC	AA		CN	CXC	CO	· CTY	י ייי	. cc1	, 4444 	וידיני	GGA	TTA
TIT C	IC GA	A TG	r TTV	, GG/	CAA	LAL		CI		. Dr.	1 1 2 2	tare	Pro	
Lys G	lu Le	u Thi	r Ast	Pro	va i	val	LAIG	CIL	, 261	FEE	, Lys	, Lys	, ,,,	,

PCT/US94/12352

WO 95/12676

28/133

P93

Sequence Range: 1 to 2102

10 20 30 40

ATG AAA AAA ATG TTA CTA ATC TTT AGT TTT TTT CTT ATT TTC TTG AAT TAC TTT TTT TAC AAT GAT TAG AAA TCA AAA AAA GAA TAA AAG AAC TTA MET Lys Lys Met Leu Leu Ile Phe Ser Phe Phe Leu Ile Phe Leu Asn>

50 60 70 80 90

GGA TTT CCT GTT AGT GCA AGA GAA GTT GAT AGG GAA AAA TTA AAG GAC CCT AAA GGA CAA TCA CGT TCT CTT CAA CTA TGG-CTT TTT AAT TTC CTG Gly Phe Pro Val Ser Ala Arg Glu Val Asp Arg Glu Lys Leu Lys Asp>

100 110 120 130 140

TTT GTT AAT ATG GAT CTT GAG TTT GTA AAT TAT AAA GGC CCT TAT GAT AAA CAA TTA TAC CTA GAA CTC : A CAT TTA ATA TTT CCG GGA ATA CTA Phe Val Asn Met Asp Leu Glu Phe Val Asn Tyr Lys Gly Pro Tyr Asp>

150 160 170 180 190

TCT ACA AAT ACA TAT GAA CAA ATA GTG GGT ATT GGG GAG TTT TTA GCA AGA TGT TTA TGT ATA CTT GTT TAT CAC CCA TAA CCC CTC AAA AAT CGT Ser Thr Asn Thr Tyr Glu Gln Ile Val Gly Ile Gly Glu Phe Leu Ala>

200 210 220 230 240

AGA CCG TTG ACC AAT TCC AAT AGC AAC TCA AGT TAT TAT GGT AAA TAT TCT GGC AAC TGG TTA AGG TTA TCG TTG AGT TCA ATA ATA CCA TTT ATA ATG Pro Leu Thr Asn Ser Asn Ser Asn Ser Ser Tyr Tyr Gly Lys Tyr>

250 260 270 280

TTT ATT AAT AGA TTT ATT GAT GAT CAA GAT AAA AAA GCA AGC GTT GAT AAA TAA TTA TCT AAA TAA CTA CTA GTT CTA TTT TTT CGT TCG CAA CTA Phe Ile Asn Arg Phe Ile Asp Asp Gln Asp Lys Lys Ala Ser Val Asp>

290 300 310 320 330

GTT TTT TCT ATT GGT AGT AAG TCA GAG CTT GAC AGT ATA TTG AAT TTA CAA AAA AGA TAA CCA TCA TTC AGT CTC GAA CTG TCA TAT AAC TTA AAT Val Phe Ser Ile Gly Ser Lys Ser Glu Leu Asp Ser Ile Leu Asn Leu>

340 350 360 370 380

AGA AGA ATT CTT ACA GGG TAT TTA ATA AAG TCT TTC GAT TAT GAC AGG TCT TCT TAA GAA TGT CCC ATA AAT TAT TTC AGA AAG CTA ATA CTG TCC Arg Arg Ile Leu Thr Gly Tyr Leu Ile Lys Ser Phe Asp Tyr Asp Arg>

FIGURE 16 (1 of 5)

							_ /		-						
	390			41	00		4	110			420			۵	30
• .	•		•		•	•		•		•	•		•	•	
TCT	AGT	GCA	GAA	TTA	דדג	CCT	270	CTT	דדמ	AC2	272	ጥኔጥ	2 አጥ	COT	CTT
NCN.	TCA	CCT	CTT	אאת	733	CCY	770	CNN	UI I	TOT.	~~~	171	WYI	CCI	CAA
AUA	100	23-	67.	77.	177	COM	110	CAA	IAA	161	iAi	YIA	TA	CGA	CAA
Ser	Ser	Ala	GIU	ren	11e	Ala	rys	vaı	He	Thr	He	Tyr	Asn	Ala	Val>
	4	140			450			46	50		4	170			480
•		•		•	•		•		•	•		•		•	•
TAT	AGA	GGA	GAT	TTG	GAT	TAT	TAT	AAA	GGG	TTT	TAT	277	Gre	CCT	CCT
ATA	TCT	CCT	AT)	244	CTA	ATA	ATA	that.	CCC	222	3773	723	~~~	001	CGA
7	7	Clar	Non	Ton	200	Th	7	7	Class	22	717		CIC	CGA	CGA
ıyı	Arg	Gry	изр	Leu	vah	ıyı	INT	Lys	CIA	Pne	:Yr	TTE	GIU	Ala	Ala>
		43	90		:	500			510		_	52	20		
	•		•	•		•		•			_		•	•	
TTA	AAG	TCT	TTA	AGT	AAA	GAA	AAT	GCA	GGT	CTT	TCT	AGG	GTT	TAT	àGT.
TAA	TTC	AGA	AAT	TCA	TTT	CTT	TTA	CGT	CCA	GAA	AGA	TCC	CAA	ATA	TC2
Leu	Lys	Ser	Leu	Ser	Lvs	Glu	λsn	Ala	Glv	Leu	Ser	Ara	Va 1	Tyr	Ser>
									,			ni g	161	131	Sei>
530			540			55	in.			560			E70		
•		•	*		•	٠,	•		•	*			570		_
CNG	TCC	CCT	CCN	220	NC N	CNA	3003			-					•
CAG	TGG	001	COM	MAG mmo	MCM mom	CAA	MIM	111	ATT	CCT	CTT	AAA	A.c.G	GAT	ATT
GIC	ACC	CGA	CCT	TTC	1G1	GTT	TAT	AAA	TAA	GGA	GYY	TTT	770	CTA	TAA
Gln	Trp	Ala	Gly	Lys	Thr	Gln	Ile	Phe	Ile	Pro	Leu	Lys	Lys	Ásp	Ile>
58	ВО		:	590			600			61	LO		6	20	
	•	•		•		•	•		•		•	•		•	
TTG	TCT	GGA	AAT	ATT	GAG	TCT	GAC	ATT	GAT	ATT	GAC	AGT	TTA	GTT	ACA
AAC	AGA	CCT	TTA	TAA	CTC	AGA	CTG	TAA	CTA	TAA	CTG	TCA	127	Cyy	700
Leu	Ser	Glv	Asn	Tle	Glu	Ser	Asp	Tle	Asn	Tle	250	Cor	Len	Unit	Thr>
		,							nap	***	עבה	Ser	rea	Vai	1>
	630			6/	10			550			<i>c</i> c n				
•	•			•	•		•	,,,,			660		_	67	, e
Chm	**	CTC	CTC	CC1	CCM	~~~	mm >								•
CON	AAG	010	010	GCA	001	CII	11A	AGT	GAA	AAT	GAA	GCA	GGT	GTT	AAC
CIA	TTC	CAC	CAC	CGT	CGA	GAA	AAT	TÇA	CTT	TTA	CII	CGT	CCA	CAA	TTG
Asp	Lys	Val	Val	Ala	Ala	Leu	Leu	Ser	Glu	Asn	Glu	Ala	Gly	Val	Asn>
	•	80			690			7(	0		7	10			723
•		•		•			•		•	•		•		•	•
TTT	GCA	AGA	GAT	ATT	ACA	GAT	ATT	CAA	GGC	GAA	ACT	CAT	AAG	GCA	GAT.
AAA	CGT	TCT	CTA	TAA	TGT	CTA	TAA	GTT	CCG	CTT	TG2	GTA	TTC	CGT	CT
Phe	Ala	Ara	Asp	Ile	Thr	Asp	Tle	Glp	Glv	Glu	Thr	uic	1	112	Asp>
									<b>-</b> -,	<b>014</b>	***-		Lys	VIG	YSDY
		73	30		-	740			750			7.0	. ^		
	•	•	•			*			,,,,			76	•		
CAA	CAT	2 2 2	አጥጥ	CAT	አጥጥ	CNA	መጠ እ	CNC		٠					
CAA	GAT	~~~	WII	CWI	WII	CAA	114	GAC	AAT	ATT	CAT	GAA	AGT	GAT	TCC
GII	CTA	TTT	IAA	CTA	TAA	CIT	AAT	CIG	TTA	TAA	GTA	CTT	TCA	CTA	AGG
Gin	Asp	Lys	Ile	Asp	Ile	Glu	Leu	Asp	Asn	Ile	His	Glu	Ser	Asp	Ser>
770			780			7	90		8	300			810		
•		•	•		•		•	•		•		•	•		•
AAT	ATA	ACA	GAA	ACT	ATT	GAA	AAT	TTA	AGG	GAT	CAG	CTT	GAA	AAA	GCT
TTA	TAT	TGT	CTT	TGA	AAT	CTT	TTA	דעע	TCC	CTA	CTC	CAA	CTT	TTTT	CCS
	101								100	CIM	$\sigma_{i}$	OV.	~	411	COA
Asn	Ile	Thr	Glu	Thr	Ile	Glu	Asn	Leu	Ara	Asp	Gln	Len	Glu	INC	Alas
Asn	Ile	Thr	Glu	Thr	Ile	Glu	Asn	Leu	Arg	Asp	Gln	Leu	Glu	Lys	Ala>

FIGURE 16 (2 of 5)

8	20		;	830			840			8	50			860	
ארא	GAT	GAA	GAG	* T40	222	*	GAG.	ልሞሞ	623	AGT	C)C	مست	CIT	•	AAA
TGT	СТА	CTT	CTC	GTA	TIT	TTT	CTC	TAA	CII	TCA	GTC	CAA	CTA	CGE	TTT
Thr	Asp	Glu	Glu	His	Lys	Lys	Glu	Ile	Glu	Ser	Gln	Val	Asp	Ala	Lys>
															-
•	870		•	8	B0 •		1	890			900		_	è	10
AAG	AAA	CAA	AAG	GAA	GAG	СТА	GAT	AAA	AAG	GCA	בדב	דע ע	منت.	C + T	AAA
TTC	TTT	GTT	TTC	CTT	CTC	GAT	CTA	TTT	TTC	CGT	TAT	TTA	GAA	CTA	TTT
Lys	Lys	Gln	Lys	Glu	Glu	Leu	Asp	Lys	Lys	Ala	Ile	Asn	Leu	Asp	Lys>
														_	_
		920			930			94	10	_		950			960
GCT	CAG	CAA	AAA	TTA	GAT	тст	GCT	C22		ኢዲሜ <sup>ቀ</sup> ፣ አልጥ		C N TO	C TV	•	•
CGA	GTC	GTT	TTT	AAT	CTA	AGA	CGA	CTT	CTA	TTA	AAT	CTA	CAL	CAA	AGA TCT
Ala	Gln	Gln	Lys	Leu	Asp	Ser	Ala	Glu	Asp	Asn	Leu	Asp	Val	Gln	Arg>
												•			
	•	91	70	•	5	980		•	990			100	70		
AAT	ACT	GTT	AGA	GAG	AAA	ATT	CAA	GAG	GAT	ATT	AAC	GAA	ATT	AAC	244
TTA	TGA	CAA	TCT	CTC	TTT	TAA	GTT	CTC	CTA	TAA	TTG	CTT	TAA	TTG	TTC
Asn	Thr	Val	Arg	Glu	Lys	Ile	Gln	Glu	Asp	Ile	Asn	Glu	Ile	Asn	Lys>
1010		1	1020			103	30		10	040			L050		
•		•	•		•		• .	•		•		•	•		•
GAA	AAG	AAT	TTA	CCA	AAG	CCT	GGT	GAT	GTA	AGT	TCT	CCT	AAA	GTT	GAT
CTT	TTC	TTA	AAT	GGT	TTC	GGA	CCA	CTA	CAT	TCA	AGA	GGA	TIT	CAA	CTA
Glu	Lys	Asn	Leu	Pro	Lys	Pro	Gly	Asp	Val	Ser	Ser.	Pro	Lys	Val	Asp>
106	50		10	070		1	1080			109	0		11	.00	
	•	•		•		•	•		•		•	•		•	
AAG	CAA	CTA	CAA	ATA	AAA	GAG	AGC	CTG	GAA	GAT	TTG	CAG	GAG	CAG	CTT
TTC	GTT	GAT	GTT	TAT	TTT	CTC	TCG	GAC	CTT	CTA	AAC	GTC	CTC	GTC	GAA
Lys	GIII	reu	Gin	116	Lys	GIU	ser	Leu	Glu	Asp	Leu	Gln	Glu	Gln	Leu>
_ 1	110			112	20		11	30		נ	140			115	0
222	CNA	300	-	C \ T	•	•	~~~	•		•	•		•		•
ተተተ	GAA CTT	AC1	CC V	CTA	CTT	TT.	CAG	AAA	AGA	GAA	ATT	GAA	AAG	CAA	ATT
Lys	Glu	Thr	Glv	Asp	Glu	Asn	Gln	LVS	Arg	Glu	TAA	CIT	TTC	GTT	TAA Ile>
-								_, _			116	GIU	Lys	GIII	116>
•	11	160		•	170			118	30	_	11	190		. 1	200
GAA	ATC	AAA	AAA	AGT	GAT	GAA	AAG	Стт	<b>ТТЪ</b>	444	እርጥ	**	CIM	• •	•
CTT	TAG	TTT	TTT	TCA	CTA	CTT	TTC	GAA	AAT	ተተተ	TCA	777	CTA	GAT.	TTT
Glu	Ile	Lys	Lys	Ser	Asp	Glu	Lys	Leu	Leu	Lys	Ser	Lys	Asp	ASD	Lys>
										_		•			-,
	•	121	•		12	220		•	1230			124	0		
GCA	AGT	AAA	GAT	GGT	AAA	GCC	TTG	GAT	<u>т</u> т	CAT	CGA	GNN	ጥጥአ	* * * **.	at Car
CGT	TCA	TTT	CTA	CCA	TTT	CGG	AAC	CTA	GAA	CTA	GCT	CTT	AII T44	TTA AAI	101
Ala	Ser	Lys	Asp	Gly	Lys	Ala	Leu	Asp	Leu	Asp	Ara	Glu	Leu	ASD	Ser>
								-		•	,				

FIGURE 16 (3 of 5)

1280 1270 1250 1260 AAA GCT TCT AGC AAA GAA AAA AGT AAA GCC AAG GAA GAA ATA ACC TTT CGA AGA TCG TTT CTT TTT TCA TTT CGG TTC CTT CTT TAT TGG Lys Ala Ser Ser Lys Glu Lys Ser Lys Ala Lys Glu Glu Glu Ile Thr> 1340 1330 1320 1310 1300 AAG GGT AAG TCA CAG AAA AGC TTA GGC GAT TTG AAT AAT GAT GAA AAT TTC CCA TTC AGT GTC TTT TCG AAT CCG CTA AAC TTA TTA CTA CTT TTA Lys Gly Lys Ser Gln Lys Ser Leu Gly Asp Leu Asn Asn Asp Glu Asn> 1370 . ----1380 1360 1350 CTT ATG ATG CCA GAA GAT CAA AAA TTA CCT GAG GTT AAA AAA TTA GAT GAA TAC TAC GGT CTT CTA GTT TTT AAT GGA CTC CAA TTT TTT AAT CTA Leu Met Met Pro Glu Asp Gln Lys Leu Pro Glu Val Lys Lys Leu Asp> 1420 1430 1410 1400 AGC AAA AAA GAA TTT AAA CCT GTT TCT GAG GTT GAG AAA TTA GAT AAG TCG TTT TTT CTT AAA TTT GGA CAA AGA CTC CAA CTC TTT AAT CTA TTC Ser Lys Lys Glu Phe Lys Pro Val Ser Glu Val Glu Lys Leu Asp Lys> 1480 1470 1460 1450 ATT TTC AAG TCT AAT AAC AAT GTT GGA GAA TTA TCA CCG TTA GAT AAA TAA AAG TTC AGA TTA TTG TTA CAA CCT CTT AAT AGT GGC AAT CTA TTT Ile Phe Lys Ser Asn Asn Asn Val Gly Glu Leu Ser Pro Leu Asp Lys> 1520 1530 1510 1500 1490 TCT TCT TAT ANA GAC ATT GAT TCA ANA GAG GAG ACA GTT ANT ANA GAT AGA AGA ATA TTT CTG TAA CTA AGT TTT CTC CTC TGT CAA TTA TTT CTA Ser Ser Tyr Lys Asp Ile Asp Ser Lys Glu Glu Thr Val Asn Lys Asp> 1570 1560 1550 GTT AAT TTG CAA AAG ACT AAG CCT CAG GTT AAA GAC CAA GTT ACT TCT CAA TTA AAC GTT TTC TGA TTC GGA GTC CAA TTT CTG GTT CAA TGA AGA Val Asn Leu Gln Lys Thr Lys Pro Gln Val Lys Asp Gln Val Thr Ser> 1620 1610 1600 1590 TTG AAT GAA GAT TTG ACT ACT ATG TCT ATA GAT TCC AGT AGT CCT GTA AAC TTA CTT CTA AAC TGA TGA TAC AGA TAT CTA AGG TCA TCA GGA CAT . Leu Asn Glu Asp Leu Thr Thr Met Ser Ile Asp Ser Ser Ser Pro Val> 1670 1660 1650 TTT TTA GAG GTT ATT GAT CCA ATT ACA AAT TTA GGA ACT CTT CAA CTT AAA AAT CTC CAA TAA CTA GGT TAA TGT TTA AAT CCT TGA GAA GTT GAA Phe Leu Glu Val Ile Asp Pro Ile Thr Asn Leu Gly Thr Leu Gln Leu>

1720 1700 1690 ATT GAT TTA AAT ACT GGT GTT AGG CTT AAA GAA AGC ACT CAG CAA GGC TAA CTA AAT TTA TGA CCA CAA TCC GAA TTT CTT TCG TGA GTC GTT CCG Ile Asp Leu Asn Thr Gly Val Arg Leu Lys Glu Ser Thr Gln Gln Gly> 1770 1760 1750 1740 1730 ATT CAG CGG TAT GGA ATT TAT GAA CGT GAA AAA GAT TTG GTT GTT ATT TAA GTC GCC ATA CCT TAA ATA CTT GCA CTT TTT CTA AAC CAA CAA TAA Ile Gln Arg Tyr Gly Ile Tyr Glu Arg Glu Lys Asp Leu Val Val Ile> 1820 1800 1790 1780 AAA ATG GAT TCA GGA AAA GCT AAG CTT CAG ATA CTT GAT AAA CTT GAA TTT TAC CTA AGT CCT TTT CGA TTC GAA GTC TAT GAA CTA TTT GAA CTT Lys Met Asp Ser Gly Lys Ala Lys Leu Gln Ile Leu Asp Lys Leu Glu> 1850 1860 1840 1830 AAT TTA AAA GTG GTA TCA GAG TCT AAT TTT GAG ATT AAT AAA AAT TCA TTA AAT TTT CAC CAT AGT CTC AGA TTA AAA CTC TAA TTA TTT TTA AGT Asn Leu Lys Val Val Ser Glu Ser Asn Phe Glu Ile Asn Lys Asn Ser> 1910 1900 1890 1880 TCT CTT TAT GTT GAT TCT AAA ATG ATT TTA GTA GCT GTT AGG GAT AAA AGA GAA ATA CAA CTA AGA TTT TAC TAA AAT CAT CGA CAA TCC CTA TTT Ser Leu Tyr Val Asp Ser Lys Met Ile Leu Val Ala Val Arg Asp Lys> 1960 1950 1940 1930 GAT AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA CTA TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT Asp Ser Ser Asn Asp Trp Arg Leu Ala Lys Phe Ser Pro Lys Asn Leu> 2000 1990 1980 1970 GAT GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT CTA CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA Asp Glu Phe Ile Leu Ser Glu Asn Lys Ile Met Pro Phe Thr Ser Phe> 2060 2050 2040 2030 TCT GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA AGA CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT Ser Val Arg Lys Asn Phe Ile Tyr Leu Gln Asp Glu Phe Lys Ser Leu> 2100 2080 2090 2070 GTT ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG TA CAA TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC AT Val Ile Leu Asp Val Asn Thr Leu Lys Lys Val Lys Xxx>

FIGURE 16 (5 of 5)

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1	TAAAAAAAT	TGTTACTAAT	CTTTAGTTTT	TTTCTTATTT	CTTTGAATGG	ATTTCCTCTT
61	አስማምር አስርርርር	AACTTCATAA	GGAAAAATTA	AAGGATTTTG	TTAATATGGA	TCTTGAGTTT
121	מדמד אמ מדמד ממדם	AAGGTCCTTA	TGATTCTACA	AATACATATG	AAÇAAATAGT	AGSTATTGGT
101	CVCLALALALADO	CAAGACCATT	GATTAATTCC	AATAGCAACT	CAATTTATTA	TGGTAAATAT
241	<b>ል</b> ተፈፈተጥልባዣጥ	GATTTATTGA	TGATCAAGAT	AAAAAAGCAA	GCGTTGATGT	TTTTTCTATT
301	CCTACTACCT	CACAGCTTGA	CAGTATATIG	AATCTAAGAA	GAATTCTTAC	AGGGTATTTG
361	עבור אובי ע ע ע ע ע ע	TTGATTATGA	AAGATCTAGT	GCTGAATTAA	TTGCTAAGGT	TATTACAATA
421	CATABITECTE	TTTATAGAGG	<b>GGATTTAAAT</b>	TATTATAAAG	AGGTTTATAT	TGAGGCTGCT
401	עבור אוים ע עיונע	TAACTAAAGA	AAATGCAGGT	CTTTCTAGAG	TGTACAGTCA	ATGGGCTGGA
541	AACACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTATAA	CTGGAAAAGT	TGAGTCTGAC
601	STALEMENTAL	ACAGTTTGGT	TACAGATAAG	GTTGTGGCAG	-ETETTTTAAG	CGAGAATGAA
661	CCACCTCTTA	ACTITICAAG	AGATATTACA	GATATTCAAG	GCGAAACTCA	TAAAGCAGAT
721	CARGATAAAA	TTGATATTGA	ATTAGATAAT	GTTCATAAAA	GTGATTCCAA	TATAACAGAG
781	ACTATTGAGA	ATTTAAGAGA	TCAGCTTGAA	AAGGCTACAG	ATGAAGAGCA	TAGAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAAGAAG	AACTAGATAA	AAAGGCAATC
907	CATCTTCATA	AAGCCCAACA	AAAATTAGAT	TCTTCTGAAG	ATAATTTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGAT	TCAAGAGGAT	ATTGACGAGA	TTAATAAAGA	AAAGAATTTG
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AGCTACAAAT	AAAAGAGAGT
1081	CTAGAAGACT	TGCAGGAACA	<b>GCTTAAAGAA</b>	ACTAGCGATG	AAAATCAAAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAGAACTTT	TAAAAAGTAA	AGATCCTAAA
1201	GCATTAGATC	TTAATGGAGA	TTTAAATTCT	AAAGTTTCTA	GTAAAGAAAA	AATTAAAGGC
1261	AAAGAAGGAG	AAATAGTCAA	AGAGGAATCA	AAGGCAAGTT	TAGCTGATTT	GAATAATGAC
1321	GAAAATCTTA	TGAGGCCGGA	AGATCAAAAA	TTATCTGAGG	TTAAAAAATT	AGATAGTAAA
1381	AAAAATTTAA	AACCTGTTTC	TGAGATTGAG	AGAGTAAATG	AAATTTCGAA	GTCTAACAAC
1441	AATGAGATTA	GTGAATCATC	ACCATTATAT	AAGCCTTCTT	ATAGCGATAT	GGATTCAAAA
1501	GAGGGTATAG	ATAATAAAGA	TGTTAACTTG	CAAGAAACCA	AGTCTCAAAC	TAAAAGTCAA
1561	CCTACTTCTT	TAAATCAAGA	. TTTGACTACT	· ATGTCTATAG	ATTCTAGTAA	TCCTGTATTT
1621	TTAGAGGTTA	TTGATCCTAT	' TACAAATTTA	GGAACGCTTC	AACTTATTGA	TTTGAATACC
1681	GGTGTTAGAC	TTAAAGAAAG	TACTCAGCAA	GCATTCAGC	GGTATGGAAT	TTATGAACGT
1741	GAAAAAGATT	TAGTTGTTAT	TAAAATGGAT	TCAGGAAAAG	CCAAGCTICA	AATACTTAAT
1801	AAACTTGAGA	ATTTAAAAGT	CATATCGGAC	TCTAATTTTG	AGATTAATAA	AAATTCATCT
1861	CTTTATGTTG	ACTOTAAAAT	GATTTTAGTA	GITGTGAGAG	ATAGTGGTAA	TGTTTGGAGA
1921	TIGGCTAAAI	TTTCTCCTA	AAATTTAAA I	GAGTTTATTC	TITCAGAGAA	TAAAATTTTG
1981	CCTTTTACTA	CCTITICICI	r GAGAAAGAA?	TTATTTATI	TGCAGGATGA	GTTTAAAAGT
2041	. CTTATTACTI	TAGATGTAA	A TACTTTAAA	AAAGTTAAGI	A	

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	•					
1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCITGITT	TTTTAAATGG	ATTTCCTCTT
61	AATGCAAGGG	AAGTTGATAA	GGAAAAATTA	AAGGACTTTG	TTAATATGGA	TCTTGAATTT
121	GTTAATTACA	AGGGTCCTTA	TGATTCTACA	GATACATATG	AACAAATAGT	AGGTATTGGG
181	<b>GAGTTTTTAG</b>	CAAGGCCGTT	GAACAATTCC	AATAGTAATT	CAAGTTATTA	TGGTAAATAT
241	TTTGTTAATA	GATTTATTGA	CGATCAAGAT	AAAAAAGCAA	GTGTTGATAT	TTTTTCTATT
301	GGTAGTAAGT	CAGAGCTTGA	TAGTATATTA	AATCTAAGAA	GAATTCTTAC	AGGGTATTTA
361	ATGAAGICTT	TTGATTATGA	GAGGTCTAGT	GCGGAATTAA	TŢĠĊŢĂĂĂĠĊ	TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTAGAT	TATTACAAAG	AGTTTTATAT	TGAGGCTTCT
481	TTGAAGTCTT	TGACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGTCA	ATGGGCTGGG
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTATAA	CTGGAAATGT	TGAGTCTGAC
				<b>GTGGTGGÇAG</b>		
661	TCAGGTGTTA	ACTITICAAG	<b>AGATATTACA</b>	GACATTCAAG	GCGAÁACTCA	TAAAGCAGAT
				TTTCATGAAA		
781	ACTATTGAGA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
				CAAAAGGAAG		
				TTTGCTGAAG		
961	GATACTGTTA	GAGAGAAGCT	TCAAGAAAAT	ATTAACGAGA	CTAATAAGGA	AAAGAATTTA
				GTTGATAAGC		
				GCTAGTGATG		
				GAAGAACTTT		
				AAAGCTTCTA		
				AAAAATTTAG		
				AATGAGGTTA		
				GAGGGTGTAG		
				CCTACTTCGT		
	0.0.0			TTAGAGGTTA		
				GGTGTTAGAC		
				GAAAAAGATT		
				AAACTCGAGA		
				CTTTATGTTG		
				TIGGCTAAAT		
				CCTTTTACTA		
			ACTTAAAAGC	TTAGTTACTT	TAGATGTAAA	TACTTTAAAA
1981	AAAGTTAAGT	Α				

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_			_			
	ATGAAAAAAA					
	AATGCAAGGG					
	GTAAACTATA					
181	GAGTTTTTAG					
241					GCGTTGATGT	
301	AGTAGTAAGT	CACAGCTTGA	CAGTATATTG	AATTTAAGAA	GAATTCTTAC	AGGGTATTTG
361	ATAAAGTCTT	TTGATTATGA	<b>AAGATCTAGT</b>	<b>GCTGAATTAA</b>	TTGCCAAGGT	TATTACAATA
421	CATAATGCTG	TTTATAGAGG	TGATTTAAAT	TATTATAAAG	AGTTTTATAT	TGAGTCTGCT
481	TTAAAGTCTT	TAACTAAAGA	AAATGCAGGT	CTTTCTAGAG	TGTACAGTCA	ATGGGCTGGA
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	AATATTTTAT	CTGGAAAAAT	TGAGTCTGAC
601	ATTGATATTG	ATAGTTTGGT	TACAGATAAG	GTTGTGGEAG	<b>CTCTTTTAAG</b>	CGAAAATGAA
661	GCAGGTGTTA	ACTITICAAG	<b>GGATATTACA</b>	GATATTCAAG	GAGAAACTCA	TAAAGCAGAT
	CAAGATAAAA					
	ACTATTGAGA					
841	ATTGAAAGTC	AAGTTGATGC	TAAAAAGAAA	CAAAAAGAAG	AACTAGATAA	AAAGGCAATC
901	GATCTTGATA	AAGCCCAACA	AAAATTAGAT	TTTTCTGAAG	ATAATTTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGAT	TCAAGAGGAT	ATTAACGAGA	TTAATAAGGA	AAAGAATTTA
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AGCTACAAAT	AAAAGAGAGT
	CTAGAAGACT					
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAGAACTTT	TAAAAAGCAA	AGATCCTAAA
1201	GCATTAGATC	TTAATCGAGA	TTTAAATTCT	AAAGCTTCTA	GTAAAGAAAA	AATTAAAGGC
1261	AAAGAAAAAG	AAATAGTCAA	AGAGAAATCA	AAGGTAAGTT	TAGGTGATTT	GGATAATGAC
1321	GAAACCCTTA	TGACGCCGGA	AGATCAAAAA	TTATCTGAGG	TTAAAAAATT	AGATAGTAAA
1381	AAAAATTTAA	AACCTGTTTC	TGAGATTGAG	AGAGTAAATG	AAATTTCAAA	GTCTAACAAC
1441	AATGAGGTTA	GCAAATCATC	ACCATTAGAT	AAGCCTTCTT	ATAGTGATAT	CGATTCAAAA
1501	GAGGTTGTAG	ATAATAAAGA	TGTTAATTTG	CAAGAAACCA	AGCCTCAAGC	TAAAAGTCAA
1561	TCTACTTCTT	TAAATCAAGA	TTTGATTACT	ATGTCTATAG	ATTCTAGTAA	TCCTGTATTT
1621	TTAGAGGTTA	TTGATCCTAT	TACAAATTTA	GGAATGCTTC	<b>AACTTATTGA</b>	TTTAAATACT
1681	GGTGTTAGAC	TTAAAGAAAG	CACTCAGCAA	GGCATTCAGC	GTTATGGAAT	TTATGAACGT
1741	GAAAAAGATT	TAGTTGTTAT	TAAAATGGAT	TCAGGAAAAG	CTAAGCTTCA	AATACTTAAT
1801	AAACTTGAGA	ATTTAAAAGT	GATATCAGAG	TCTAATTTTG	AGATTAATAA	AAATTCATCT
1861	CTTTATGTTG	ACTCTAAAAT	GATTTTAGTA	GCTGTGAAAG	ATAGTGGTAA	TGTTTGGAGA
1921	TTGGCTAAAT	TTTCTCCTAA	AAATTTAGAT	GAGTTTATTC	TTTCAGAGAA	TAAAATTTTG
1981	CCTTTTACTA	GCTTTTCTGT	GAGAAAGAAT	TTTATTTATT	TGCAAGATGA	GTTTAAAAGT
2041	CTTATTACTT	TAGATGTAAA	TACTTTAAAA	AAAGTTAAGT	A	

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1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCTIGITI	TTTTAAATGG	ATTTCCTCTT
61	DODACODAKA	AACTTGATAA	GGAAAAATTA	AAGGACTTTG	TTAATATGGA	TCTTGAATTT
121	CTTAATTACA	AGGGTCCTTA	TGATTCTACA	AATACATATG	AACAAATAGT	AGGTATTGGG
181	GAGTTTTTAG	CAAGGCCGTT	GATCAATTCC	AATAGTAATT	CAAGTTATTA	TGGTAAATAT
241	ATAATTSYTTE	CATTTATTCA	CGATCAAGAT	AAAAAAGCAA	GTGTTGATAT	TTTTTCTATT
301	CCTACTAAGT	CAGAGCTTGA	TAGTATATTA	AATCTAAGAA	GAATTCTTAC	AGGGTATTTA
361	ATGAAGTCTT	TTGATTATGA	GAGGTCTAGT	GCGGAATTAA	TTGCTAAAGC	TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTAGAT	TATTACAAAG	AGTTTTATAT	TGAGGCTTCT
481	TTGAAGTCTT	TGACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGTCA	ATGGGCTGGG
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTTAT	CTGGAAATGT	TGAGTCTGAC
601	ATTGATATTG	ATAGTTTGGT	TACAGATAAG	GTGGTGGÇAG	CICLILITYYC	TGAGAATGAA
661	TCAGGTGTTA	ACTITICAAG	<b>AGATATTACA</b>	GACATTCAAG	GCGAAACTCA	TAAAGCAGAT
721	CAAGATAAAA	TTGATATTGA	ATTAGATAAT	ATTCATGAAA	GTGATTCCAA	TATAACAGAA
781	ACTATTGAGA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	Taaaaaagag
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
901	GATCTTGATA	AAGCTCAACA	AAAATTAGAT	TTTGCTGAAG	ATAATCTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGCT	TCAAGAGAAT	ATTAACGAGA	CTAATAAGGA	AAAGAATTTA
1021	CCAAAGCCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AACTACAAAT	AAAAGAGAGC
1081	CTGGAAGATT	TGCAGGAGCA	GCTTAAAGAA	ACTGGTGATG	AAAATCAGAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAAAGCTTT	TAAAAAGTAA	AGATGATAAA
1201	GCAAGTAAAG	ATGGTAAAGC	CTTGGATCTT	GATCGAGAAT	TAAATTCTAA	AGCTTCTAGC
1261	AAAGAAAAA	GTAAAGCCAA	GGAAGAAGAA	ATAACCAAGG	GTAAGTCACA	GAAAAGCTTA
1321	GGCGATTTGA	ATAATGATGA	AAATCTTATG	ATGCCAGAAG	ATCAAAAATT	ACCTGAGGTT
1381	AAAAAATTAG	ATAGCAAAAA	AGAATTTAAA	CCTGTTTCTG	AGGTTGAGAA	ATTAGATAAG
1441	ATTTTCAAGT	CTAATAACAA	TGTTGGAGAA	TTATCACCGT	TAGATAAATC	TTCTTATAAA
1501	GACATTGATT	CAAAAGAGGA	GACAGITAAT	AAAGATGTTA	ATTTGCAAAA	GACTAAGCCT
1561	CAGGTTAAAG	ACCAAGTTAC	TTCTTTGAAT	GAAGATTTGA	CTACTATGTC	TATAGATTCC
1621	AGTAGTCCTG	TATTTTTAGA	GGTTATTGAT	CCAATTACAA	ATTTAGGAAC	TCITCAACIT
1681	ATTGATTTAA	ATACTGGTGT	TAGGCTTAAA	GAAAGCACTC	AGCAAGGCAT	TCAGCGGTAT
1741				GTTATTAAAA		
1801				AAAGTGGTAT		
				AAAATGATTT		
1921	GATAGTAGTA	ATGATTGGAG	ATTGGCCAAA	TITICICCIA	AAAATTTAGA	TGAGTTTATT
				AGCTTTTCTG		
2041	TTGCAAGATC	AGTITAAAAG	TCTAGTTATT	TTAGATGTAA	ATACTTTAAA	AAAAGTTAAG
2101	TAAAGCC					

## p93 - pKO

1	АТСААААААА	TGTTACTAAT	CTTTAGTTTT	TTTCTTGTTT	TTTTAAATGG	ATTICCICIT
	2200022000	A ACTIVE ATTA A	CCAAAAATTA	AAGGACTTIG	TTAATATGGA	TUTTGAATTT
-01	CONTRACTOR CA	V CCCALCLALD	ACATALACTA ACTA	AATACATATG	AACAAATAGT	WGG1W11GG
181	CACCOMMENTALLYC	C & ACCIOCITY	CATTAATTCC	AATAGTAATI	CAAGITATTA	1001WWWIWI
241	WILLY VALVANAMA	COLLEGALLE	CGATCAAGAT	AAAAAAGCAA	GIGITGATAT	TITITUMIT
201	COMPOUNDACE	CACACCTTCA	TACTATATTA	AATCTAAGAA	GAATICITAC	AGGGTATTTA
263	Putch P Calculate	TYPATTATY A	GAGGTCTAGT	GCGGAATTAA	TIGCIAAAGC	TATTACAATA
422	CALCAN VANCANC	COACALALA	ACATTTAGAT	TATTACAAAG	AGITITATAT	TGAGGCTTCT
401	THANKS & CALCALA	TCACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGICA	ATGGGCTGGG
E 47	226767676	J. Metre datable du	TYTTAAAAAG	AATATTTTAT	CIGGAAAIGI	TGAGTCTGAC
241	MACACACAAA	PAPELLIA CA	TACAGATAAG	GTGGTGGCAG	CICTITIAAG	TGAGAATGAA
001	WITCHINITO	VIVOITIOOT	AGATATTACA	GACATTCAAG	GCGAAACTCA	TAAAGCAGAT ·
001	TUAGGIGIIA	WCITIOCHIO	ATTAGATAAT	TTTCATGAAA	GTGATTCCAA	TATAACAGAA
721	CAAGATAAAA	TIGHTHIAG	TC ACCOMICA A	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
781	ACTATIGAGA	WITTHHOOGH	TONOCITODI	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
841	ATTGAAAGTC	AGGIIGAIGC	TACATTAGAG	TTTGCTGAAG	ATAATCTAGA	TATTCAAAGG
901	GATCTTGATA	ANGCI CANCA	TOATIAGAI	ATTAACGAGA	CTAATAAGGA	AAAGAATTTA
	GATACTGTTA	CHOHOHNOC1	1Caronnari	CTTCATAAGC	AGTTGCAGAT	AAAAGAGAGT
1021	CCAAAGCCIG	GIGNIGITUG	CCTTAAACAA	GCTAGTGATG	AAAATCAAAA	AAGAGAAATA
1081	CTAGAAGATT	TOCAMONGCA	TANDAGE CACAC	CAAGAACTTT	TTAAAAATAA	AGATCATAAA
1141	GAAAAGCAAA	TIGAMATCAA	TATALICA CAME	AAACCTTCTA	GTAAAGAAAA	AATTGAAGGC
1201	GCATTAGATC	1 1 MAGCAAGA	ACATACTAAA	DATTTAGAGA	AGCCTGTTTC	TGAGGCTGAT
1261	GAAGAAGAGG	WINNAGANII	CACADACTOC	ATTENCETTA	GTAAATTATC	CCCGTTAGAT
1321	AAAGTAGATA	AMAITICCAN	TC1MCMC	CACCCTCTAG	ATAACAAAGA	TGTTGATTTG
1381	GAGCCTTCTT	ATAGCGACAT	TOWN TOWN		TAAATGAAGA	CTTGATTGAT
1441	CAAAAAACTA	AACCCCAAGI	TOWNO 1 CV	TTACACCTTA	TCGATCCGAT	TACAAATTTA
1501	GIGICIATAG	ATTUCAGIAA	. 1001010111 11666777777	CCTCTTAGAC	TTAAAGAAAG	TGCTCAACAA
1561	GGAACGCTTC	AACTIATIOA	1110001000	CAAAAACATT	TGGTTGTTAT	TAAAATAGAT
	GGTATTCAGC	GATATGGAAT	CARACTTCAT	· AAACTCGAGA	ATTTAAAAGT	GATATCAGAG
1681	TCAGGAAAAG	CIAAGCIICA	CWINCIIONI	THE TENER THE T	ACTOTAGAAT	CATTTTACTA
1741	TCTAATTTIG	AGATTAATAA	WWWIICHIC!	מממרת מודים ו	TTTCTCCTAA	AAATTTAGAT
1801	GITGITAAGG	ACGATAGTAA	TOCTIONWAY	: Chalandaria : Tiggerswer	CCTTTGCTGT	GAGAAAGAAT
1861	GAATTTATIC	TOTCAGAAAA	, 1444411110	TOTALIACIA	AAATOTADA	TACTITAAAA
			ACTIMAMAGE	. IINGIINCI	. ANGRAGIANA	
1981	AAAGTTAAGT	. <b>A</b>				

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				TTP COMPANY	J. J. L.	July Market
1	ATGAAAAAAA	TGTTACTAAT	CTTTAGTTTT.	ALICIANIA	TTT ATTACTO	actacycatate
61	ATGAAAAAA AATGCAAGGA	AAGTTGATAA	GGAAAAATTA	AAGGATTIG	YYCY YYDOU	CCCTATACCC
			WALK ALLA ALLA LAND	DIMINA		COLLIACO
		~ N N ~ N ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	CyCCyyntel(C)	AATAGCAACI	CUNCTIVITU	IOCUMINI
041		U CAlab Kutalab K U	יוים זע מיצעייצעי		GIGIIGAIGI	****
201	TRESCONDE	CACACCTACA	CACTATATY	AATTTAAGAA	GWWIICIIWC	VOCATUTUTU
361	ATAAAGTCTT	TCGATTATGA	CAGGTCTAGT	GCAGAATTAA	TIGCIMAGGI	TAT TACAMIA
421	TATAATGCTG	TTTATAGAGG	AGATTTGGAT	TATTATAAAG	GGTTTTATAT	TUNGCCIGCI
481	TTGAAGTCTT	TAACTAAAGA	AAACGCAGGT	CTTTCTAGGG	TTTACAGICA	GIGGGCIGGW
F 43	E E ESTATA	J. Make Garden & C.	TYTTAAAAAG	GATATTTTGT	CIGGAAATAT	TURATUTUAL
CAI	ALL CONCURATION	y Cy Catalatic Cal.	TACAGATAAG	GTGATAGCAG	CICITITIAAG	CONVAVATORY
re-	CCACCCCTTA	PCALALACC P PC	AGATATTACA	GATATICAAG	GCGAAACICA	TAAGGCAGAT
771	CARCATARCA	TTYCATACTYCA	ATTAGACAAT	ATCCATGAAA	GCGATTCTAA	TATAACAGAA
701	Z C C STYPE CTO Z	PATALYPICCEY	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
041	AMMONANCITO	ACCURCATIC	ТАААААСААА	.GAAAAGGAAG	AGCTAGATAA	AAAGGCAATC
001	A DAY TATE OF A	AACCTCACCA	AAAATTAGAC	TCTGCTGAAG	ATAATITAGA	TGTTCAAAGA
061	CAMPONALD	CACACAAAAT	TCAAGAGGAT	ATTAATGAGA	TTAATAAGGA	AAAGAATTIG
7021	CCANANCCTC	CTCATCTAAG	TTCTCCTAAA	GTTGATAAGC	AACTGCAAAT	AAAAGAGAGT
1001	CUPCAPCEAL	TOPACTACION	CCTTAAAGAA	GCTGGTGATG	AAAATCAGAA	AAGAGAAATT
1141	CACAACCAAA	TYPEAAATYAA	AAAAAGGGAC	GAAGAACTTT	TAAAAAGTAA	AGATGGCAAA
1201	CTABCTABAC	ATTATGAAGC	ATTAGATCTT	GATCGAGAAT	TATCCAAAGC	TICIAGIAAA
1261	CANANANCTA	ACCTYCAACCA	AGAAGAAATA	ACTAAAGGTA	AATCACGGGC	AAGCTTAGGC
1221	CATTTCAATA	AAAAAAAAA	CCTTATGTTG	CCAGAAGATC	AAAAATTACC	TGAAGATAAA
1321	AAATTGGATA	GTAAATTAGA	TGGTAAAAAA	GAATTTAAAC	CAGITICIGA	GGTTGAAAAA
1441	TTAGATAAGA	TTTCCAAGTC	TAATAACAAT	GAGGTTGGCA	AGTTATCACC	ATTAGATAAG
1501	CCTTCTTATY	ATGATATTGA	TTCAAAAGAG	GAGGTAGATA	ATAAAGCTAT	TAATTTGCAA
1561	AAGATCGACC	CTAAAGTTAA	AGACCAAACT	ACTICITIGA	ATGAAGATTT	GGATAAAGAT
1621	TITEDATACTA	TGTCTATAGA	TTCCAGCAGT	CCTGTATTTC	TAGAGGITAT	TGATCCTATT
1691	ACAAATTTAG	CAACCCTGCA	GCTTATTGAT	` TTAAATACTG	GGGTTAGGCT	TAAGGAAAGC
1741	ACTYACEAAC	CCATTCAGCG	GTATGGAATI	' TATGAACGTG	AAAAAGATTT	GGTTGTTATT
1801	AAAATGGATT	CAGGAAAGGC	TAAGCTTCAA	ATACTTAATA	AGCTTGAAAA	TTTGAAAGTG
1861	CTATYAGAGT	CTAATTTTGA	CATCAATAA?	<i>NATTCATCTC</i>	TTTATGTTGA	CICTAAAAIG
1921	ATTITICCAC	CTGTTAGAGA	TAAGGATGAT	' AGCAATGCTT	' GGAGATTGGC	TAAATTTTCT
1001	ריים בל בל בל בל	TCCATCACTT	TATTCTTTC	GAGAATAAAA	TTTTGCCTTT	TACTAGCTTT
2041	TOTAL PARTY	AAAATTTTAT	TTATTTGCA	GATGAGCTTA	AAAATCTAGT	TATTTTAGAT
210	GTAAATACTT	רסממממת	TAAGTA			
210.	GIVVVIVCI	TANADANO				

#### K48 OSP A/ PGAU OSP A FUSION

39/*13*3

		10	0			20			30			4	0		
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAA	TAT	TTA	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
TAC	TTT	TTT	ATA	AAT	AAC	CCT	TAT	CCA	GAT	TAT	AAT	CGG	AAT	TAT	CGT
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	λla>
50			60			•	70			80			90		
		•		~~~	•		•	•	<b></b>	•		•	•		•
TGT	AAG	CAA	AAT.	CAA	AGC	AGC	CIT	GAT	GAA	AAA	-AAT	AGC	GTT	TCA	GTA .
Ove.	Tare	GID	114	Va l	Ser	Sor	LAN	CIM	CIT	111	TTA	TCG	CAA	AGT	CAT Val>
Cys	Lys	GIII	Yell	Val	261	261	Dea	wsb	GIU	Lys	ASII	ser	Val	Ser	Val>
10	00			110			120			1:	30		;	140	
	*	*		•		•	•		•		*	•		•	
GAT	TTA	CCT	GGT	GGA	ATG	ACA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	አአአ
ACD	AAT	GGA	CLA	Clar	MAC	TGT	CAA	GAA	CAT	TCA	TTT	CTT	TTT	CIG	TTT
nsp	Den	PIO	GIY	GIY	nec	Int	vai	Leu	vaı	ser	Lys	GIU	Lys	Asp	Lys>
	150			16	50		:	170			180			19	90
•	•		•		•	•		•		•	•		•		•
GAC	GGT	AAA	TAC	AGT	CTA	GAG	GCA	ACA	GTA	GAC	AAG	CIT	GAG	CTT	AAA
CIG	CCA	TIT	ATG	TCA	GAT	CTC	CGT	TGT	CAT	CTG	TTC	GAA	CIC	GAA	TTT
ASD	GIY	Lys	Tyr	ser	Leu	GIU	ATG	Inr	val	Asp	Lys	Leu	Glu	Leu	Lys>
	2	200			210			22	20		•	230			240
•		•		•	•		•		•	•		•		•	•
GGA	ACT	TCT	GAT	• AAA	AAC	AAC	GGT	TCT	• GGA	ACA	CTT	GAA	GGT	• GAA	AAA
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT	CCA	CTT	AAA TTT
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT	CCA	CTT	AAA
CCT	ACT TGA	TCT AGA	CTA Asp	TTT	AAC TTG Asn	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT	CCA Gly	CTT	AAA TTT
Gly	ACT TGA Thr	TCT AGA Ser	CTA Asp	TTT Lys	AAC TTG Asn	TTG Asn 260	CCA Gly	TCT AGA Ser	GGA CCT Gly 270	TGT	CTT GAA Leu	GAA CTT Glu	CCA Gly	CTT Glu	AAA TTT Lys>
CCT Gly ACT	ACT TGA Thr	TCT AGA Ser 25	CTA Asp 50 • AGT	TTT Lys	AAC TTG Asn	TTG Asn 260	CCA Gly TTA	TCT AGA Ser	GGA CCT Gly 270	TGT Thr	CTT GAA Leu	GAA CTT Glu _28	CCA Gly 80 • CTA	CTT Glu	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25 AAA TTT	CTA Asp  0 AGT TCA	TTT Lys AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT	CCA Gly TTA AAT	TCT AGA Ser	GGA CCT Gly 270 ATT TAA	TGT Thr GCT CGA	CTT GAA Leu • GAT CTA	GAA CTT Glu _28 GAC CTG	CCA Gly 80 • CTA GAT	CTT Glu • AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA Thr	ACT TGA Thr GAC CTG	TCT AGA Ser 25 AAA TTT	CTA Asp  0 AGT TCA Ser	TTT Lys AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT	CCA Gly TTA AAT	TCT AGA Ser	GGA CCT Gly 270 ATT TAA	TGT Thr GCT CGA	CTT GAA Leu • GAT CTA	GAA CTT Glu _28 GAC CTG	CCA Gly 80 • CTA GAT	CTT Glu • AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25 AAA TTT	CTA Asp  0 AGT TCA	TTT Lys AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT	CCA Gly TTA AAT Leu	TCT AGA Ser	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA	CTT GAA Leu • GAT CTA	GAA CTT Glu _28 GAC CTG	CCA Gly 80 • CTA GAT	CTT Glu • AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA Thr	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA Asp 60 AGT TCA Ser 300	Lys  AAA TTT Lys	AAC TTG Asn GTA CAT Val	AAA TTT Lys	CCA Gly TTA AAT Leu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala	CTT GAA Leu GAT CTA Asp	GAA CTT Glu 28 GAC CTG Asp	CCA Gly 30 CTA GAT Leu	CTT Glu AGT TCA Ser	AAA TIT Lys> CAA GTT Gln>
ACT TGA Thr	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA ASP  O AGT TCA Ser  300 GAA	Lys  AAA TTT Lys  ATT	AAC TTG Asn GTA CAT Val	ASD ASD AAA TTT Lys AAA	CCA Gly TTA AAT Leu IO	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320	CTT GAA Leu GAT CTA Asp	GAA CTT Glu 28 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330	CTT Glu AGT TCA Ser	AAA TIT Lys> CAA GTT Gln>
ACT TGA Thr 290 • ACT TGA	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val	TTG ASN 260 AAA TTT Lys 31	CCA Gly TTA AAT Leu GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GCC CGG	TGT Thr GCT CGA Ala 320 AAA TTT	CTT GAA Leu GAT CTA Asp	GAA CTT Glu .28 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330 GTA CAT	CTT Glu AGT TCA Ser TCA AGT	AAA TIT Lys> CAA GIT Gln> AAA TIT
ACT TGA Thr 290 • ACT TGA	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val	TTG ASN 260 AAA TTT Lys 31	CCA Gly TTA AAT Leu GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GCC CGG	TGT Thr GCT CGA Ala 320 AAA TTT	CTT GAA Leu GAT CTA Asp	GAA CTT Glu .28 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330 GTA CAT	CTT Glu AGT TCA Ser TCA AGT	AAA TIT Lys> CAA GTT Gln>
ACT TGA Thr 290 • ACT TGA	ACT TGA Thr GAC CTG Asp AAA TTT Lys	TCT AGA Ser 25 AAA TTT Lys	CTA Asp 50 AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val	TTG ASN 260 AAA TTT Lys 31	CCA Gly TTA AAT Leu GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GCC CGG	GCT CGA Ala 320 AAA TTT Lys	CTT GAA Leu GAT CTA Asp	GAA CTT Glu .28 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	CTT Glu AGT TCA Ser TCA AGT	AAA TIT Lys> CAA GIT Gln> AAA TIT
ACT TGA Thr TGA TCT TGA Thr	ACT TGA Thr GAC CTG Asp AAA TTT Lys	TCT AGA Ser 25 AAA TTT Lys TTT AAA Phe	CTA ASP  O AGT TCA Ser  300 CTT GAA CTT Glu	AAA TTT Lys ATT TAA Ile	AAC TTG ASD GTA CAT Val TTC AAG Phe	AAA TTT Lys AAA TTT Lys	CCA Gly TTA AAT Leu GAA CTT Glu 360	TCT AGA Ser ACA TGT Thr GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys	GAT CTA ASP ACA TGT Thr	GAA CTT Glu .28 GAC CTG Asp TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser	AAA TIT Lys> CAA GTT Gln> AAA TTT Lys>
ACT TGA Thr TGA Thr ACT TGA Thr	ACT TGA Thr GAC CTG Asp AAA TTT Lys	TCT AGA Ser 25 AAA TTT Lys TTT AAA Phe	CTA ASP  O AGT TCA Ser  300 GAA CTT Glu  CTT	AAA TTT Lys ATT TAA Ile	AAC TTG ASD GTA CAT Val TTC AAG Phe	AAA TTT Lys AAA TTT Lys AAA TTT AAA TTT AAA AAA AAA AAA AAA AA	CCA Gly TTA AAT Leu GAA CTT Glu 360	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys GAA	GAT CTA ASP ACA TGT Thr	GAA CTT Glu .28 GAC CTG Asp TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser	AAA TIT Lys> CAA GIT Gln> AAA TIT Lys>
ACT TGA Thr TGA Thr ACT TGA Thr	ACT TGA Thr GAC CTG Asp AAA TTT Lys	TCT AGA Ser 25 AAA TTT Lys TTT AAA Phe ACC TGG	CTA ASP  O AGT TCA Ser  300 GAA CTT Glu  CTT GAA	AAA TTT Lys ATT TAA Ile 50 AAA TTT	AAC TTG ASN GTA CAT Val TTC AAG Phe GAC CTG	AAA TTT Lys AAA TTT Lys AAA TTT Lys AAG TTC	CCA Gly TTA AAT Leu GAA CTT Glu 360 TCA AGT	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys GAA CTT	GAT CTA ASP ACA TGT Thr	GAA CTT Glu .28 GAC CTG Asp TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser	AAA TIT Lys> CAA GIT Gln> AAA TIT Lys>

FIGURE 23 (1 of 3)

K48 OSP A/ PGAU OSPA FUSION

	390			40	0		4	10	•		420			43	0
•	•		•		•	•		•		*	•		•		•
AAG	GGT	GAA	ACA	TCT	GAA	AAA	ACA	ATA	GTA	AGA	GCA	TAA	GGA	ACC	AGA
TTC	CCA	CTT	TGT	AGA	CTT	TTT	TGT	TAT	CAT	TCT	CGT	TTA	CCI	TGG	TCT
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
					450		•	46	:n		Α	70			480
	4	140		•	450		•	4.	•	•	•	•		•	*
CTT	GAA	TAC	ACA	GAC	ATA	AAA	AGC	GAT	GGA	TCC	GGA	AAA	GCT	AAA	GAA
GAA	CTT	ATG	TGT	CTG	TAT	TTT	TCG	CTA	CCT	AGG	CCT	TTT	CGA	TTT	CTT :
Leu	Glu	Tyr	Thr	Asp	Ile	Lys	Ser	Asp	Gly	Ser	Gly	Lys	Ala	Lys	Glu>
			90			00			510			52	0		
	•	4.	• .	•	-	•		•	*		•	-	•	•	
GTT	TTA	AAA	GAC	TTT	ACT	CTT	GAA	GGA	ACT	CTA	GCT	GCT	GAC	GGC	AAA
CAA	AAT	TTT	CTG	AAA	TGA	GAA	CTT	CCT	TGA	GAT	CGA	CGA	CIG	CCG	TIT
Val	Leu	Lys	Asp	Phe	Thr	Leu	Glu	Gly	Thr	Leu	Ala	Ala	Asp	Gly	Lys>
530			540			5.5	50		9	60			570		
-		•	•		•	-	•	•		•		•	•		•
ACA	ACA	TTG	AAA	GTT	ACA	GAA	GGC	ACT	GTT	GTT	TTA	AGC	AAG	AAC	λTT
TGT	TGT	AAC	TTT	CAA	TGT	CTT	CCG	TGA	CAA	CAA	TAA	TCG	TTC	TTG	TAA
Thr	Thr	Leu	Lys	Val	Thr	Glu	Gly	Thr	Val	Val	Leu	Ser	Lys	Asn	Ile>
5	RA		:	590			600			61	LO			620	
5	80	•	;	590		•	600		•	61	LO	•	(	5 <b>20</b>	
TTA	• AAA	• TCC	GGA	GAA	ATA	• ACA	GTT	GCA	CTT	GAT	• GAC	* TCT	GAC	ACT	ACT
TTA AAT	AAA TTT	AGG	GGA CCT	GAA CTT	TAT	TGT	GTT CAA	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA	TGA
TTA AAT	AAA TTT	AGG	GGA CCT	GAA CTT	TAT	TGT	GTT CAA	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA	ACT TGA Thr>
TTA AAT	AAA TTT Lys	AGG Ser	GGA CCT	GAA CTT Glu	TAT	TGT	GTT CAA Val	CGT Ala	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA Thr	TGA
TTA AAT Leu	AAA TTT Lys 630	AGG Ser	GGA CCT Gly	GAA CTT Glu	TAT Ile 40	TGT Thr	GTT CAA Val	CGT Ala 650	GAA Leu	GAT CTA Asp	GAC CTG Asp	AGA Ser	GAC CTG Asp	ACT TGA Thr	TGA Thr>
TTA AAT Leu .	AAA TTT Lys 630	AGG Ser	GGA CCT Gly	GAA CTT Glu 6	TAT Ile 40 ACT	TGT Thr	GTT CAA Val	CGT Ala 650 TGG	GAA Leu GAT	GAT CTA Asp	GAC CTG Asp 660	AGA Ser ACT	GAC CTG Asp	ACT TGA Thr 67	TGA Thr> 70 TTA
TTA AAT Leu CAG	AAA TTT Lys 630 GCT	AGG Ser	GGA CCT Gly	GAA CTT Glu 6 AAA TTT	TAT Ile 40 ACT TGA	TGT Thr GGA CCT	GTT CAA Val	CGT Ala 650 TGG	GAA Leu GAT CTA	GAT CTA Asp TCA	GAC CTG Asp 660 AAA TTT	AGA Ser ACT TGA	GAC CTG Asp TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA AAT
TTA AAT Leu CAG	AAA TTT Lys 630 GCT	AGG Ser	GGA CCT Gly	GAA CTT Glu 6 AAA TTT	TAT Ile 40 ACT TGA	TGT Thr GGA CCT	GTT CAA Val	CGT Ala 650 TGG	GAA Leu GAT CTA	GAT CTA Asp TCA	GAC CTG Asp 660 AAA TTT	AGA Ser ACT TGA	GAC CTG Asp TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA
TTA AAT Leu CAG	AAA TTT Lys 630 GCT	AGG Ser ACT	GGA CCT Gly	GAA CTT Glu 6 AAA TTT	TAT Ile 40 ACT TGA	TGT Thr GGA CCT Gly	GTT CAA Val	CGT Ala 650 TGG ACC	GAA Leu GAT CTA	GAT CTA Asp TCA	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA	GAC CTG Asp TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA AAT
TTA AAT Leu  CAG GTC Gln	AAA TTT Lys 630 GCT CGA	AGG Ser ACT TGA Thr	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 * ACT TGA Thr	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp	GAA Leu GAT CTA Asp	GAT CTA Asp * TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr	GAC CTG Asp * TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr	TGA Thr> 70 TTA AAT Leu>
TTA AAT Leu  CAG GTC Gln	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 ACT TGA Thr 690	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7	GAA Leu GAT CTA ASP	GAT CTA ASP TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA
TTA AAT Leu CAG GTC Gln ACA	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 ACT TGA Thr 690	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7	GAA Leu GAT CTA Asp	GAT CTA ASP TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	ACT TGA Thr 710 GTG	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT
TTA AAT Leu CAG GTC Gln ACA	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 ACT TGA Thr 690	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7	GAA Leu GAT CTA Asp	GAT CTA ASP TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	ACT TGA Thr 710 GTG	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA
TTA AAT Leu CAG GTC Gln ACA	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6 AAA TTT Lys	TAT Ile 40 ACT TGA Thr 690	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7	GAA Leu GAT CTA Asp	GAT CTA ASP TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser TGA Thr 710 GTG CAC	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT
TTA AAT Leu CAG GTC Gln ACA TGT	AAA TTT Lys 630 CGA CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC	TAT Ile  40  ACT TGA Thr  690  ACC ACC ACC ACC ACC ACC ACC ACC ACC A	GGA CCT Gly AAA TTI Lys	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7 ACT TGA TTGA	GAA Leu GAT CTA ASP 00 ACA TGT Thr	GAT CTA ASP TCA AGT Ser CAA GTT	GAC CTG ASP 660 AAA TTT Lys CTT GAA Leu	ACT TGA Thr 710 GTG CAC	GAC CTG Asp TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>
TTA AAT Leu  CAG GTC G1n ACA TGT Thx	AAA TTT Lys 630 GCT CGA Ala ATT	AGG Ser ACT TGA Thr 680 C AGI	GGA CCT Gly AAA TTT Lys CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC AST	TAT Ile  40  ACT TGA Thr  690  AGC AGC AGC AGC AGC AGC AGC AGC AGC AG	GGA CCT Gly AAA TTI Lys	GTT CAA Val AAA TTT Lys	CGT Ala 650	GAA Leu GAT CTA ASP 00 ATGT Thr	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG ASP 660 AAA TTT Lys CTT GAA Leu	AGA Ser  ACT TGA Thr  710 • GTG CAC Val	GAC CTG Asp TCT AGA Ser TTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr ACT TGA Thr ACT TGA Thr ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>
TTA AAT Leu  CAG GTC G1n ACA TGT Thx	AAA TTT Lys 630 GCT CGA Ala ATT TAA	AGG Ser ACT TGA Thr 680 C AGI C Ser	GGA CCT Gly AAA TTT Lys CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC AST	TAT Ile  40  ACT TGA Thr  690  AGC AGC AGC AGC AGC AGC AGC AGC AGC AG	GGA CCT Gly AAA 740	GTT CAA Val AAA TTT Lys AAA TTT Lys	CGT Ala 650 TGG ACC Trp 77 ACT TGA TAX	GAA Leu GAT CTA ASP 00 ATGT Thr	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser  ACT TGA Thr  710 CAC Val	GAC CTG	ACT TGA Thr 67 ACT TGA Thr TGA Thr TGA Thr TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>

FIGURE 23 (2 of 3)

#### K48 OSPA / PGAU OSP A FUSION

770 780 790 800 810

GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT
CTT CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA
Glu Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asr. Ala>

820

TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 23 (3 of 3)

## B-31 OSP A /PGAU OSP A FUSION

10	n	20	30		40 .
		•	• •	•	• •
ATG AAA AAA	TAT TTA TTG	GGA ATA	GGT CTA	ATA TTA GCC	TTA ATA GCA
	sms እአጥ አአሮ	CCT TAT	CCA GAT	INI WWI COC	WI INI COI
Met Lys Lys	Tyr Leu Leu	Gly Ile	Gly Leu	Ile Leu Ala	Leu Ile Ala>
				80	90
50	60	70	•		• • .
* *	• • • • • • • • • • • • • • • • • • •	AGC CTT	GAT GAA	AAA AAC AGO	GCT TCA GTA
	መመኔ ሮኔክ ፕሮር	TICG GAA	CIA CII	111 110 100	CON NOT CHE
ACG TIC GIT	Asn Val Ser	Ser Leu	Asp Glu	Lys Asn Sex	Ala Ser Val>
Cys bys oin					
100	110	120		130	140
• •	•	• •	*	10m 111 Ch	, ,,, cac ,aa
GAT TTG CCT	GGT GAG ATC	AAA GTT	CTT GIA	TO THE CT	A AAA GAC AAA T TTT CTG TTT
CTA AAC GGA	CCA CTC TAG	TIT CAA	tou Val	Ser Lys Gl	TTTT CTG TTT Lys Asp Lys>
Asp Leu Pro	GIA GIR WE	Lys var	Dea var	<b> </b>	
150	160		170	180	190
		•	•	• •	• •
GAC GGT AAG	TAC AGT CT.	A AAG GCA	ACA GTA	GAC AAG AT	T GAG CTA AAA
	አምር ጥርክ ርክ	ኮ ጥጥር ርርገ	r TGT CAI	CIG TIC IN	W CIC GWI III
Asp Gly Lys	Tyr Ser Le	u Lys Ala	Thr Val	Asp Lys II	e Glu Leu Lys>
		•	220	230	240
200	. 21		•		• •
רכא ארת תרת	CAT AAA GA	C AAT GG	T TCT GG	A GTG CTT GA	A GGT ACA AAA
151	CALL WALL CA	C TTA CC	A AGA CC	I CAC GAA CI	I CCV IGT ITT
Gly Thr Ser	Asp Lys As	p Asn Gl	y Ser Gly	y Val Leu Gl	u Gly Thr Lys>
•					280
2	50	260	27	• •	* *
•	• • • • • • • • • • • • • • • • • • •	י די מממ מי	ACA AT	T GCT GAC G	AT CTA AGT AAA
	, mcs mmm c	ነጥ ጥጥጥ እአ	T TGT TA	W COW CIG C	IN GNI ICH III
Acn Acn Ive	Ser Lvs Al	a Lys Le	u Thr Il	e Ala Asp A	sp Leu Ser Lys>
Wah wah mia	, 501 5,0	<u>-</u>			
290	300	310		320	330
• •	• •		•		TA CTC TCA AGA
ACC ACA TTO	GAA CTT T	ra aaa ga	VA GAT GG	1 TOT TOT A	TA GTG TCA AGA AT CAC AGT TCT
TGG TGT AAC	G CTT GAA A	AT TIT C	lu Asp G	v Lvs Thr L	eu Val Ser Arg>
Thr Thr Phe	e Glu rea r	eu Lys G.	Lu Nop o		
340	350	3	60	370	380
•	•	•	•	• •	• •
AAA GTA AG	T TCT AGA G	AC AAA A	CA TCA A	CA GAT GAA	TG TTC AAT GAA
	A ACA TOT C	ידר דידר די	CT AGT TY	GT CTA CII	TAC AAG IIA CII
Lys Val Se	r Ser Arg A	sp Lys T	hr Ser T	nr Asp Glu	det Phe Asn Glus

FIGURE 24 (1 of 3)

## B-31 OSP A/ PGAU OSP A FUSION

	•	390			40	0		4	10			420			43	C
	•	•		•		•	•		•		•	~ .		•		•
	AAA	GGT	GAA	TTG	TCT	GCA	AAA	ACC	A1G	ACA TOT	AUA	CTT	ተ ተ	CCT	WCC.	AAA AAA
	TTT	CCA	CTT	AAC	AGA	NID	THE	The	Mar	Thr	Arc	Glu	) tru	Gly	Thr	Lys>
	Lys	GIÄ	GIU	ren	ser	WIG	Lys	1111	Mec	1111	nr 9	014	no	013	2 444	Lysz
	•	4	140			450			46	0		4	70			460
	•		•		•	•		•	۰. ۳	•	•	~~	•		•	•
	CTT	GAA	TAT ATA	ACA	GAA	ATG	AAA	AGC	CTA	CCT	ACC TCT	CCT CCT	AAA	CC3	AAA	CAA
	GAA	CTT	ATA	TGT	CIT	TAC	111	Cor	CIM	Gly	The	CLI	Tare	λla	7.70	Glu>
	Leu	GIU	ıyr	Thr	GIU	met	гуs	261	vəħ	GIY	****	013	<i>D</i> , 3	AIG	د ړپ	0242
			49	90		5	00			510			52	20		
		•		•	•		•		•	•		•		•	•	
	GTT	TTA	AAA	AAG	TTT	ACT	CTT	GAA	GGA	AAA	GTA	GCT	AAT	GAT	AAA	GTA
	CAA	AAT	TTT	TTC	AAA	TGA	GAA	CTT	CCT	TTT	CAT	CGA	TTA	CTA	TIT	CAT
	Val	Leu	Lys	Lys	Phe	Thr	Leu	Glu	Gly	Lys	Val	λla	Asn	Asp	Lys	Val>
	530			540			5!	50		9	560			570		
	•		•	•		•		*	•		•		•	•		•
	ACA	TTG	GAA	GTA	AAA	GAA	GGA	ACC	GTT	ACT	TTA	AGT	AAG	GAA	ATT	GCA
	TGT	AAC	CTT	CAT	TTT	CTT	CCT	TGG	CAA	TGA	AAT	TCA	TTC	CTT	TAA	CGT
	Thr	Leu	Glu	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Glu	Ile	Ala>
	- 51	80			590			600			6	10			620	
	_	•	•		•		•	•		•		•	•		•	
	AAA	TCT	GGA	GAA	GTA	ACA	• GTT	• GCT	CTT	AAT	GAC	ACT	AAC	ACT	ACT	CAG
	AAA TTT	TCT	CCT	GAA CTT	GTA CAT	TGT	CAA	GCT CGA	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA	GTC
	AAA TTT	TCT	CCT	GAA CTT	GTA CAT	TGT	CAA	GCT CGA	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA	CAG GTC Gln>
	AAA TTT	TCT	CCT	GAA CTT	GTA CAT Val	TGT	CAA	GCT CGA Ala	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA Thr	GTC
	AAA TTT Lys	TCT AGA Ser	Gly	GAA CTT Glu	GTA CAT Val	TGT Thr 40	CAA Val	GCT CGA Ala	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	TTG Asn	ACT TGA Thr	ACT TGA Thr	GTC Glm>
	AAA TTT Lys	TCT AGA Ser 630	Gly	GAA CTT Glu	GTA CAT Val 6	TGT Thr 40	CAA Val	GCT CGA Ala	GAA Leu 650 GAT	TTA Asn TCA	GAC CTG Asp	ACT TGA Thr 660	TTG Asn TCT	ACT TGA Thr	ACT TGA Thr 6	GTC Glm> 70 * ACA
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630	Gly AAA	GAA CTT Glu AAA	GTA CAT Val 6 ACT TGA	TGT Thr 40 • GGC CCG	CAA Val GCA CGT	GCT CGA Ala TGG ACC	GAA Leu 650 GAT CTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	TTG Asn TCT AGA	ACT TGA Thr ACT TGA	ACT TGA Thr 6' TTA AAT	GTC Glm> 70 * ACA TGT
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630	Gly AAA	GAA CTT Glu AAA	GTA CAT Val 6 ACT	TGT Thr 40 • GGC CCG	CAA Val GCA CGT	GCT CGA Ala TGG ACC	GAA Leu 650 GAT CTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	TTG Asn TCT AGA	ACT TGA Thr ACT TGA	ACT TGA Thr 6' TTA AAT	GTC Glm> 70 * ACA
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630	Gly AAA	GAA CTT Glu AAA	GTA CAT Val 6 ACT	TGT Thr 40 • GGC CCG	CAA Val * GCA CGT Ala	GCT CGA Ala TGG ACC	GAA Leu 650 GAT CTA Asp	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	TTG Asn TCT AGA	ACT TGA Thr ACT TGA	ACT TGA Thr 6' TTA AAT	GTC Glm> 70 * ACA TGT
	AAA TTT Lys • GCT CGA Ala	TCT AGA Ser 630 ACT TG/	CCT Gly AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA Asp	TCA AGT AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA	TTG Asn TCT AGA Ser 710	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6 TTA AAT Leu	GTC Glm> 70 * ACA TGT Thr>
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680	GAA CTT Glu	GTA CAT Val  6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA Asp	TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu	GTC Glm> 70 * ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680	GAA CTT Glu . AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7	TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu AAA TTT	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT
•	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680	GAA CTT Glu . AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7	TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu AAA TTT	GTC Glm> 70 * ACA TGT Thr> 720
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680 T GTT A CAA	GAA CTT Glu . AAA TTT Lys	GTA CAT Val  6 ACT TGA Thr	TGT Thr 40 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7	TCA AGT Ser	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA TGA Thr	TCT AGA Ser 710 TTTT AAA	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 6' TTA AAT Leu AAA TTT	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT
	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680 GTI A CAA	GAA CTT Glu . AAA TTT Lys . AAC . TTO . Asr	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 GGC CCG Gly 690 AAA TTI Lys	GCA Val GCA CGT Ala AAA TTI Lys	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7 ACA TGI	TCA AGT Ser OO CAA GTT	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser 710 . TTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr	ACT TGA Thr 6 TTA AAT Leu AAA TTT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT Gln>
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 680 CAA Val	GAA CTT Glu AAA TTT Lys AAC	GTA CAT Val  6 ACT TGA Thr	TGT Thr  40 • GGC CCG Gly 690 • AAA TTT Lys	GCA CGT Ala AAA TTI Lys 740	GCT CGA Ala TGG ACC Trp	GAA Leu 650 GAT CTA ASP 7 ACA TGI Thi	TTA Asn TCA AGT Ser 00 CAA GTT GTT TS0	GAC CTG ASP AAAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr CGTG CAC	TTG Asn  TCT AGA Ser  710  TTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr	ACT TGA Thr 6 TTA AAT Leu AAA TIT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT Gln>
-	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thi	CCT Gly AAA TTT Lys 680 CAA CAA Val	GAA CTT Glu AAA TTT Lys AAC AC	GTA CAT Val  6 ACT TGA Thr AGG TCG	TGT Thr  40 GGC CCG Gly 690 AAA TTT	GCA CGT Ala AAA TTI Lys 740 CAA CGT	GCT CGA Ala TGG ACC Trp ACT TGA TGA TGA	GAA Leu 650 GAT CTA ASP 7 ACA TGI Thi	TTA Asn TCA AGT Ser 00 CAA GTT TSG TCG TCG TCG TCG TCG TCG TCG TCG TCG TC	GAC CTG ASP AAAA TTT Lys GAA CTI CGA CGC GCC GCC GCC GCC GCC GCC GCC GCC	ACT TGA Thr 660 ACT TGA Thr CAC Val	TTG Asn  TCT AGA Ser  710  TTTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr ACT ACT ACT ACT ACT TGA	ACT TGA Thr 6° TTA AAT Leu AAA TIT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT Gln>

FIGURE 24 (2 of 3)

B-31 OSP A /PGAU OSP A FUSION

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820

AAT AAA TTA TTT

Lys \*\*\*>

PCT/US94/12352 **WO** 95/12676

B31/K48 fusion 40 20 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 80 90 50 60 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 130 120 110 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 190 160 170 180 150 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 230 240 220 200 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 270 280 260 250 GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 300 310 320 330 290 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 380 360 340 350 AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TTT CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTA CTT Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu> 430 400 410 420

> AAA GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GAC GGA ACC AGA TTT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT Lys Gly Glu Val Ser Glu Lys Ile Ile Thr Arg Ala Asp Gly Thr Arg>

390

FIGURE 25 (1 of 2)

B31/K48 fusion 480 450 CTT GAA TAC ACA GGA ATT AAA AGC GAT GGA TCT GGA AAA GCT AAA GAG GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 520 500 510 GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAN ANT TIT CCG ATA CAN GAN CIT CCT TGN GAT TGN CGN CIT TIT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr> =::::: 550 560 540 530 ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser> 600 610 590 580 AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 660 670 630 GCT ACT AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA CGA TGA TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT Ala Thr Lys Lys Thr Ala Ala Trp Asn Ser Lys Thr Ser Thr Leu Thr> 720 700 710 680 690 ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys Glu> 750 760 730 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA GAA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT CTT Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu> 780 790 800 810 770 GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

PCT/US94/12352

47/133

### B-31 OSP A/ 25015 OSP A FUSION

	10			20			30			-4	10		
•	•	•		•		•	•		•		•	•	
ATG AAA													
TAC TTT : Met Lys !	TTT ATA	AAT	AAC	CCT	TAT	CCA	CAT	TAI	TAN	Ala	LAU	TAL	Alas
met Lys	Lys lyi	Leu	rea	GIY	116	GIĀ	Den	116	Leu	VIC	Deu	-16	WIG>
50	60	)		7	0			80			90		
. •	•	•	•		•	•		•		•	•		•
TGT AAG													
ACA TTC													
Cys Lys	Gln Asr	val	Ser	Ser	Leu	Asp	Glu	Ly_s.	.Asn	Ser	Val	Ser	Val>
100		110			120			13	20		•	140	
100	•	110		•	120		•		•	•	-	•	
GAT TTG	CCT GG	GAA	ATG	AAA	GTT	CTT	GTA	AGC	AAA	GAA	AAA	AAC	AAA
CTA AAC	GGA CC	CTT	TAC	TTT	CAA	GAA	CAT	TCG	TTT	CTT	TTT	TTG	TTT
Asp Leu	Pro Gly	/ Glu	Met	Lys	Val	Leu	Val	Ser	Lys	Glu	Lys	Asn	Lys>
150		1.	60			170			180			19	20
150	•	11	*	•	-	•		•	100		•	13	•
GAC GGC	AAG TAG	GAT	CTA	ATT	GCA	ACA	GTA	GAC	AAG	CTT	GAG	CTT	AAA
CTG CCG													
Asp Gly	Lys Ty	. Asp	Leu	Ile	Ala	Thr	Val	Asp	Lys	Leu	Glu	Leu	Lys>
2	00		210			25	20			วรก			240
. 2	00	•	210		•	22	20	•	:	230		•	240
GGA ACT	•	• 444	•	TAA	• GGA		•	• GTA		•	GGC	GTA	•
GGA ACT	TCT GA'	A TTT	AAC TTG	TTA	CCT	TCT AGA	• GGA CCT	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA TTT
GGA ACT	TCT GA'	A TTT	AAC TTG	TTA	CCT	TCT AGA	• GGA CCT	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA TTT
GGA ACT	TCT GA' AGA CT Ser As	A TTT	AAC TTG Asn	TTA Asn	CCT	TCT AGA	GGA CCT Gly	CAT	CTT GAA	GAA CTT Glu	CCG	CAT	AAA TTT
GGA ACT	TCT GA'	A TTT	AAC TTG Asn	TTA	CCT	TCT AGA	• GGA CCT	CAT	CTT GAA	GAA CTT Glu	CCG	CAT	AAA TTT
GGA ACT CCT TGA Gly Thr	TCT GAAAGA CT. Ser As	A TTT p Lys .	AAC TTG Asn	TTA Asn 260 AAA	CCT Gly TTA	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu	GAA CTT Glu 2	CCG Gly 80 • CTA	CAT Val	AAA TTT Lys>
GGA ACT CCT TGA Gly Thr GCT GAC CGA CTG	TCT GA' AGA CT Ser As  250 AAA AG TTT TC	A TTT  D Lys  A AAA  A TTT	AAC TTG Asn GTA	TTA ASD 260 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GGA ACT CCT TGA Gly Thr	TCT GA' AGA CT Ser As  250 AAA AG TTT TC	A TTT  D Lys  A AAA  A TTT	AAC TTG Asn GTA	TTA ASD 260 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp	TCT GA' AGA CT Ser As  250 AAA AG TTT TC Lys Se	A TTT  D Lys  T AAA  A TTT  T Lys	AAC TTG Asn GTA	TTA ASD 260 AAA TTT Lys	CCT Gly TTA AAT Leu	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA Ser	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT Leu	CAT Val GGT CCA	AAA TTT Lys>
GGA ACT CCT TGA Gly Thr GCT GAC CGA CTG	TCT GA' AGA CT Ser As  250 AAA AG TTT TC	A TTT  D Lys  T AAA  A TTT  T Lys	AAC TTG Asn GTA	TTA ASD 260 AAA TTT Lys	CCT Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 2 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA	TCT GA' AGA CT Ser As  250 AAA AG TTT TC Lys Se  30 CTT GA	A TTT D Lys T AAA A TTT T Lys O A GTT	AAC TTG Asn GTA CAT Val	TTA Asn 260 AAA TTT Lys 3	TTA AAT Leu  GAA	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330	CAT Val GGT CCA Gly	AAA TTT Lys> CAA GTT Gln>
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA TGG TGT	TCT GA' AGA CT Ser As  250  AAA AG TTT TC Lys Se  30  CTT GA GAA CT	A TTT C Lys T AAA A TTT T Lys O A GTT T CAA	AAC TTG ASn GTA CAT Val	AAA AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA	TCT GA' AGA CT Ser As  250  AAA AG TTT TC Lys Se  30  CTT GA GAA CT	A TTT C Lys T AAA A TTT T Lys O A GTT T CAA	AAC TTG ASn GTA CAT Val	AAA AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA TGG TGT Thr Thr	TCT GA' AGA CT Ser As  250  AAA AG TTT TC Lys Se  30  CTT GA GAA CT	A TTT D Lys I AAA A TTT T Lys O A GTT T CAA U Val	AAC TTG ASn GTA CAT Val	AAA AAA TTT	TTA AAT Leu  GAA CTT Glu	TCT AGA Ser ACA TGT Thr GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA TGG TGT	TCT GA' AGA CT Ser As  250  AAA AG TTT TC Lys Se  30  CTT GA GAA CT	A TTT C Lys T AAA A TTT T Lys O A GTT T CAA	AAC TTG ASn GTA CAT Val	AAA AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG Asp	GAA CTT Glu 2 GAT CTA ASP	CCG Gly 80 CTA GAT Leu 330 GTA CAT Val	GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA TGG TGT Thr Thr  340 AAA GTA	TCT GAAAAAGA CT CAAAAAAAAAAAAAAAAAAAAAAA	A TTT D Lys I AAA A TTT T Lys O A GTT T CAA U Val 350	AAC TTG ASn GTA CAT Val TTC AAG Phe	AAA TTT Lys AAA TTT Lys AAA TTT Lys	CCT Gly  TTA AAT Leu  10  GAA CTT Glu  360	TCT AGA Ser ACA TGT Thr GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys 3	GAC CTG ASP ACA TGT Thr	GAA CTT Glu 2 GAT CTA ASP CTA GAT Leu	CCG Gly 80 CTA GAT Leu 330 GTA CAT Val	GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
GGA ACT CCT TGA Gly Thr  GCT GAC CGA CTG Ala Asp  290 ACC ACA TGG TGT Thr Thr  340	TCT GA' AGA CT Ser As  250 AAA AG TTT TC Lys Se  30 CTT GA GAA CT Leu Gl  ACT TGA	A TTT D Lys I AAA A TTT T Lys A GTT T CAA U Val 350 C AAA	AAC TTG ASn GTA CAT Val TTC AAG Phe	AAA TTT Lys AAA TTT Lys AAA TTT Lys	CCT Gly  TTA AAT Leu  10 GAA CTT Glu  360 • TCA	TCT AGA Ser ACA TGT Thr CTA Asp	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser 320 AAA TTT Lys 3	GAC CTG ASP ACA TGT Thr	GAA CTT Glu 2 GAT CTA ASP CTA GAT Leu	CCG Gly 80 CTA GAT Leu 330 GTA CAT Val	GGT CCA Gly TCA AGT Ser 380	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>

FIGURE 26 (1 of 3)

### B-31 OSP A/ 25015 OSP A FUSION

AAA GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GCA GGA ACC AGA TTT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT Lys Gly Glu Val Ser Glu Lys Ile Ile Thr Arg Ala Asp Gly Thr Arg>  440
Lys Gly Glu Val Ser Glu Lys Ile Ile Thr Arg Ala Asp Gly Thr Args   440
CTT GAA TAC ACA GGA ATT AAA AGC GAT GGA TCT GGA AAA GCT AAA GAG GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu>  490 500 510 520  GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr> 530 540 550 560 570  ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser> 580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 630 640 650 660 670
GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu>  490 500 510 520  GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr>  530 540 550 560 570  ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu>  490 500 510 520  GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr>  530 540 550 560 570  ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr>  530
CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr>  530
CAA AAT TTT CCG ATA CAA GAA CTT CCT TGA GAT TGA CGA CTT TTT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr>  530
530 540 550 560 570  ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser>  580 590 600 610 620  AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 630 640 650 660 670 GCT ACT AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala>  630 640 650 660 670  GCT ACT AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
630 640 650 660 670 GCT ACT AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
GCT ACT AAA AAA ACT GCA GCT TGG AAT GCA GGC ACT TCA ACT TTA ACA
CGA TGA TTT TTT TGA CGT CGA ACC TTA CGT CCG TGA AGT TGA AAT TGT
Ala Thr Lys Lys Thr Ala Ala Trp Asn Ala Gly Thr Ser Thr Leu Thr>
680 690 700 710 720
ATT ACT GTA AAC AAC AAA AAA ACT AAA GCC CTT GTA TTT ACA AAA CAA TAA TGA CAT TTG TTG TTT TTT TGA TTT CGG GAA CAT AAA TGT TTT GTT
Ile Thr Val Asn Asn Lys Lys Thr Lys Ala Leu Val Phe Thr Lys Gln>
730 740 750 760
GAC ACA ATT ACA TCA CAA AAA TAC GAC TCA GCA GGA ACC AAC TTG GAA CTG TGT TAA TGT AGT GTT TTT ATG CTG AGT CGT CCT TGG TTG AAC CTT
Asp Thr Ile Thr Ser Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu>

FIGURE 26 (2 of 3)

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### B-31 OSP A/ 25015 OSP A FUSION

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA
CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT
Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

AGA TCT Arg>

FIGURE 26 (3 of 3)

### K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		1	0		:	20			30			4	0		
	•		•	•		•		•	•		-		<u>-</u>		
ATG	AAA	AAA	TAT	ATT	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
				A P T	<b>3.2C</b>	CCT	TAT	CCA	GAL	IWI	W	600	nn:	4114	COL
Mot	ivs	Ivs	Tvr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	Ala>
1100	2, 2	_, _	٠,												
εń			60			7	0			80			90		
50		•			•		•	•		*		• .	•		•
		CNA	አእጥ	СТТ	AGC	AGC	CTT	GAT	GAA	AAA	AAT	AGC	GTT	TCA	GTA
			mm k	CAA	TCC	TCG	CAA	CTA	CIT	7.7.1.	TIM	100	CAA	MOI	CAL.
ACA	TIC	GTT	11W	UAA	Sor	Car	t.eu	ASD	Glu	Lys	Asn	Ser	Val	Ser	Val>
Cys	Lys	Gin	ASN	AGI	261	361	200			-•					
							120			1	30			140	
10	00			110			120		•	_	•	*		•	
	•	•					-	~~~	CTA	λCT	444	GAA	AAA	GAC	AAA
GAT	TTA	CCI	GGT	GGA	ATG	ACA	GTT.	CII	CIN	TO1	delete trans	Cutati	Arter.	CTG	THE
CTA	AAT	GGA	CCA	CCT	TAC	TGT	CAA	GAA	CAL	104		C11	Tue	200	Tyes
Asp	Leu	Pro	Gly	GJA	Met	Thr	Val	Leu	Val	Ser	rys	GIU	Lys	vsh	Lys>
	150	)		1	60			170			180		_	1	90
•	•		•		•	•		•		•					
GAC	GGT	. AA	TAC	AGT	CTA	GAG	GCA	ACA	GTA	GAC	AAG	CIT	GAG	CFI	' እእአ ተተተ
			· > T/C	ጥርእ	CAT	•  ርጥር	CGT	TGI	CA		111	. GAA		GAA	
Asp	Gly	Lys	Tyr	Ser	Lev	Glu	Ala	Thr	Va)	. Asp	Lys	Leu	Glu	Leu	Lys>
	2		-												_
		200			210	)		2	220			230			240
	,			•	•	•	•		•	1	•	•		•	•
cc	א ארי	г тс	r GA	נגג ז	AAC	AAC	GG7	TC	r GG	A AC	A CT	C GAP	GGT	GAZ	AAA A
			N CT	4	r ጥጥ(	: TTC	CC	A AG	A CC	r TG	r GAZ	7 CT1	· CCP	CI	
Cla	· Th	r Se	r Asi	Lv	s Ası	a Asr	Gly	/ Se	r G1	y Thi	r Lei	ı Glu	ı Gly	Glı	Lys>
GI	, 111.		,												
			250			260			27	0		2	280		
	•		•		•	•		•		*	•		•	•	•
	T C N	~ AA	A AG	т аа	A GT	A AA	TT	A AC	TA A	T GC	T GA	T GAG	CT	A AG	T CAA
		~ ~~	~ ~~	N TT	T CA'	T TY	ቦ ልል'	r TG	Т ТА	A CG	A Cr	A CIT	j GA:	1 10	W GII
16	~ <b>~</b>	5 II	- Se	r tv	s Va	l Lv:	s Le	u Th	r Il	e Al	a As	p As	p Le	ı Se	r Gln>
ın	r AS	p by	3 36	,	• • •										
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290			50				•		•	*		•		•	•
		. m	~ C	א איז	-T TT	~ AA	A GA	A GA	T GC	C AA	A AC	A TT	A GT	A TC	ጸዳል <i>ል</i> ።
			. ~	wn 472		C TT	ጥ ሮሞ	$\tau$ $\sim$	'A CC	:G 77	T TU	T AA	TCA	I We	M
TG	A TI	T A	AA CI	T 18	יי איי	0 11	. G1	11 Ac	n Al	a L	's Th	r Le	u Va	1 Se	r Lys>
Th	r Ly	/S Pl	ie Gl	Lu II	e Pf	ic D	. GI			1	•				
				200			36	. n			370			380	)
	340			350	,	_	26				•		•		•
	•		•	·				·	~ A . A .	Ch C	AA G	וא או	רד ב	C A	AC GAA
£A.	AA G	ra at	cc c	TT A	AA GA	AC AA	IG TO	.A 1	-W W	-A C	יים היים	ואו עולן בי ניי	T A	יני טי	AC GAA NG CTT
T	rt C	T TA	GG G	AA T	TT C	rg Ti	C AC	- A		P	11 0	1,, 5.	,	10 A	rG CTT
L	ys V	al T	hr L	eu L	ys A	sp L)	s Se	er S	er T	III G	Lu G.	ru r)	a Pi	1 L	sn Glu>

FIGURE 27 (1 of 3)

K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

430 400 390 AAG GGT GAA ACA TCT GAA AAA ACA ATA GTA AGA GCA AAT GGA ACC AGA TTC CCA CTT TGT AGA CTT TTT TGT TAT CAT TCT CGT TTA CCT TGG TCT Lys Gly Glu Thr Ser Glu Lys Thr Ile Val Arg Ala Asn Gly Thr Arg> 480 470 460 450 CTT GAA TAC ACA GAC ATA AAA AGC GAT GGA TCC GGA AAA GCT AAA GAA GAA CTT ATG TGT CTG TAT TTT TCG CTA CCT AGG-CCT TTT CGA TTT CTT Leu Glu Tyr Thr Asp Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 520 510 500 490 GTT TTA AAA GAC TTT ACT CTT GAA GGA ACT CTA GCT GCT GAC GGC AAA CAA AAT TTT CTG AAA TGA GAA CTT CCT TGA GAT CGA CGA CTG CCG TTT Val Leu Lys Asp Phe Thr Leu Glu Gly Thr Leu Ala Ala Asp Gly Lys> 560 550 530 ACA ACA TTG AAA GTT ACA GAA GGC ACT GTT GTT TTA AGC AAG ATT TCA TGT TGT AAC TTT CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TAA AGT Thr Thr Leu Lys Val Thr Glu Gly Thr Val Val Leu Ser Lys Ile Ser> 610 600 590 580 AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 650 670 660 640 630 GCT ACT AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA CGA TGA TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT Ala Thr Lys Lys Thr Ala Ala Trp Asn Ser Lys Thr Ser Thr Leu Thr> 710 700 680 690 ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys Glu> 760 750 740 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA GAA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT CTT Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu>

FIGURE 27 (2 of 3)

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K48 OSP A / B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTA TTT

Lys \*\*\*>

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### B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		1	0			20			30			. 4	0		÷
ATC	*	AAA	• TAT	* 4TT	<b>ተ</b> ፕር	400	ATA	• GGT	CTA	АТА	TTA	GCC	TTA	* ATA	CC2
		TTT													
Met	Lys	Lys	Tyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	Ala>
50			60			-	70			80			90		
•		•	•		•		•	•		•		•	•		•
		CAA													
		GTT													CAT Val>
cys	Lys	GIII	N>11	AGI	361	SEL	Dea	vsħ	GIU	Lys	ASII	361	AGI	261	Val>
10	00		1	110			120			13	30		:	140	
C) T	•	CCT	CCT	CCA	እጥር	*	<b>*</b>	ርጥጥ	• CTN	»CT	*	~ ~ ~		•	•••
		GGA													
															Lys>
	150			3.4	50			70			100				
•	150		•	7.0	•	•		170		•	180		•	19	•
GAC	GGT	AAA	TAC	AGT	CTA	GAG	GCA	ACA	GTA	GAC	AAG	CTT	GAG	CTT	AAA
		TTT													
Asp	Gly	Lys	Tyr	Ser	Leu	Glu	Ala	Thr	Val	Asp	Lys	Leu	Glu	Leu	Lys>
	:	200			210			2:	20		:	230			240
		*	·	•	•		•		•	•		•		•	•
	ACT	· TCT			AAC			TCT	• GGA		CTT	GAA			AAA
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT	CCA	CTT	AAA
CCT	ACT TGA	TCT AGA Ser	CTA Asp	TTT	AAC TTG Asn	TTG Asn	CCA	TCT AGA	GGA CCT Gly	TGT	CTT GAA	GAA CTT Glu	CCA Gly	CTT	AAA TTT
CCT	ACT TGA	TCT AGA Ser	CTA	TTT	AAC TTG Asn	TTG	CCA	TCT AGA	GGA CCT	TGT	CTT GAA	GAA CTT Glu	CCA	CTT	AAA TTT
CCT Gly ACT	ACT TGA Thr	TCT AGA Ser 2:	CTA Asp 50 AGT	TTT Lys	AAC TTG Asn	TTG Asn 260 AAA	CCA Gly TTA	TCT AGA Ser	GGA CCT Gly 270	TGT Thr	CTT GAA Leu	GAA CTT Glu 21	CCA Gly 30 • CTA	CTT Glu	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA ASP 50 AGT TCA	TTT Lys • AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT	CCA Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	TGT Thr GCT CGA	CTT GAA Leu GAT CTA	GAA CTT Glu 21 GAC CTG	CCA Gly 30 CTA GAT	CTT Glu AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA ASP 50 AGT TCA	TTT Lys • AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT	CCA Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA	TGT Thr GCT CGA	CTT GAA Leu GAT CTA	GAA CTT Glu 21 GAC CTG	CCA Gly 30 CTA GAT	CTT Glu AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA ASP 50 AGT TCA	TTT Lys • AAA TTT	AAC TTG Asn GTA CAT	TTG Asn 260 AAA TTT Lys	CCA Gly TTA AAT	TCT AGA Ser • ACA TGT	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA	CTT GAA Leu GAT CTA	GAA CTT Glu 21 GAC CTG	CCA Gly 30 CTA GAT	CTT Glu AGT TCA	AAA TTT Lys>
CCT Gly ACT TGA Thr	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300	TTT Lys • AAA TTT Lys	AAC TTG Asn GTA CAT Val	TTG Asn 260 AAA TTT Lys	CCA Gly TTA AAT Leu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala	CTT GAA Leu GAT CTA Asp	GAA CTT Glu 2 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330	CTT Glu AGT TCA Ser	AAA TTT Lys> CAA GTT Gln>
CCT Gly ACT TGA Thr 290	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 2: AAA TTT Lys	CTA Asp 50 AGT TCA Ser 300	TTT Lys AAA TTT Lys	AAC TTG Asn GTA CAT Val	TTG Asn 260 AAA TTT Lys 3	TTA AAT Leu  10 GAA	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320	CTT GAA Leu GAT CTA ASP	GAA CTT Glu 2 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330	CTT Glu AGT TCA Ser	AAA TTT Lys> CAA GTT Gln> AAA
ACT TGA Thr	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val TTC AAG	TTG Asn 260 AAA TTT Lys 3: AAA TTT	TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TGT Thr GCT CGA Ala 320	CTT GAA Leu GAT CTA ASP	GAA CTT Glu 2 GAC CTG Asp	CCA Gly 80 CTA GAT Leu 330 GTA CAT	CTT Glu AGT TCA Ser TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA
ACT TGA Thr 290 ACT TGA Thr	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu	Lys  AAA TTT Lys  ATT TAA Ile	AAC TTG Asn GTA CAT Val TTC AAG	TTG Asn 260 AAA TTT Lys 3: AAA TTT	TTA AAT Leu 10 GAA CTT Glu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	GCT CGA Ala 320 AAA TTT Lys	CTT GAA Leu GAT CTA Asp	GAA CTT Glu 2 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser	AAA TTT Lys> CAA GTT Gln>
ACT TGA Thr 290 ACT TGA Thr	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 2: AAA TTT Lys	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys ATT TAA	AAC TTG Asn GTA CAT Val TTC AAG	TTG Asn 260 AAA TTT Lys 3: AAA TTT	TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	GCT CGA Ala 320 AAA TTT Lys	CTT GAA Leu GAT CTA ASP	GAA CTT Glu 2 GAC CTG Asp	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	CTT Glu AGT TCA Ser TCA AGT	AAA TTT Lys> CAA GTT Gln>
ACT TGA Thr 290 ACT TGA Thr ACT ACT ACT ACT ACT ACT ACT ACA AAA	ACT TGA Thr GAC CTG ASP AAA TTT Lys	TCT AGA Ser 2: AAA TTT Lys TTT AAA Phe	CTA ASP 50 AGT TCA Ser 300 CTT Glu	LYS  AAA TTT LYS  ATT TAA Ile  350	AAC TTG Asn GTA CAT Val	TTG Asn 260 AAA TTT Lys AAA TTT Lys AAA ATTT AAA AAA	CCA Gly  TTA AAT Leu  10  GAA CTT Glu  360  TCA	TCT AGA Ser . ACA TGT Thr . GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys 3	CTT GAA Leu GAT CTA ASP ACA TGT Thr	GAA CTT Glu 2 GAC CTG Asp TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
ACT TGA Thr 290 ACT TGA Thr ACT TGA TTT	ACT TGA Thr GAC CTG ASP AAA TTT Lys	TCT AGA Ser 2: AAA TTT Lys TTT AAA Phe ACC TGG	CTA ASP 50 AGT TCA Ser 300 GAA CTT Glu CTT GAA	AAA TTT Lys  ATT TAA Ile  350 AAA TTT	AAC TTG Asn GTA CAT Val TTC AAG Phe GAC CTG	TTG Asn 260 AAA TTT Lys AAA TTT Lys AAA TTT T	CCA Gly TTA AAT Leu 10 GAA CTT Glu 360 • TCA	TCT AGA Ser ACA TGT Thr GAT CTA ASP	GGA CCT Gly 270 ATT TAA Ile GCC CGG Ala	GCT CGA Ala 320 AAA TTT Lys GAA CTT	CTT GAA Leu GAT CTA ASP ACA TGT Thr	GAA CTT Glu 2 GAC CTG Asp TTA AAT Leu	CCA Gly 30 CTA GAT Leu 330 GTA CAT Val	AGT TCA Ser TCA AGT Ser 380	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>

FIGURE 28 (1 of 3)

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### B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

	390			40	0		4	110			420			4:	30 .
•	•		•		•	•		. •	•	•	•		•		•
										AGA					
										TCT					
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
	4	40			450			46	50		4	70			480
•		•		•	. •		•		•	•		•		•	•
										TCC					
										AGG					
Leu	Glu	Tyr	Thr	Asp	Ile	Lys	Ser	Asp	Gly	Sër'	Gly	Lys	Ala	Lys	Glu>
		49	90		5	500	•		510			52	20		
	•		•	*		•		•	•		•		•	•	
										CTA					
										GAT					
Val	Leu	Lys	ASP	Pne	inr	Leu	613	GIA	Inr	Leu	Ala	ATG	ASP	GIA	Lys>
530			540			55	50		5	560			570		
•		•	•		•		•	•		•		•	•		•
			-							GTT					
										CAA					
Thr	Thr	Leu	Lys	Val	Thr	Glu	Gly	Thr	Val	Val	Leu	Ser	Lys.	Ile	Ser>
58	B0		!	590			600			6:	10		•	520	
	•	•		•		•	•		•		•	•		•	
AAA	TCT		GAA	GTT			GAA			GAC	• ACT		AGT	AGT	
AAA TTT	TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TTT	TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	
AAA TTT	TCT AGA	CCC	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA Ser	CGA
AAA TTT Lys	TCT AGA Ser 630	CCC	GAA CTT Glu	GTT CAA Val	AGT Ser 40	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TTT Lys	TCT AGA Ser 630 ACT	CCC Gly	GAA CTT Glu	GTT CAA Val 6-	AGT Ser 40 • GCA	CAA Val	GAA CTT Glu TGG	GAA Leu 650 *	TTA Asn TCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala> 70 ACA
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 6- ACT TGA	AGT Ser 40 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	CTG Asp TCC AGG	AGT TCA Ser • ACT TGA	AGT TCA Ser 67	CGA Ala> 70 + ACA TGT
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 6- ACT TGA	AGT Ser 40 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	CTG Asp TCC AGG	AGT TCA Ser • ACT TGA	AGT TCA Ser 67	CGA Ala> 70 ACA
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT	GAA CTT Glu • AAA TTT	GTT CAA Val 6- ACT TGA	AGT Ser 40 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 * AAT TTA Asn	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG	AGT TCA Ser • ACT TGA	AGT TCA Ser 67	CGA Ala> 70 + ACA TGT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6. ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn	TTA Asn TCA AGT Ser	GAC CTG Asp • AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6. ACT TGA Thr	AGT Ser 40 • GCA CGT Ala 690 •	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Txp	GAA Leu 650 AAT TTA Asn 7	TTA Asn TCA AGT Ser 00	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
AAA TTT Lys GCT CGA Ala ATT	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6. ACT TGA Thr AGC TCG	AGT Ser 40 GCA CGT Ala 690 CAA GTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TTP	GAA Leu 650 AAT TTA ASD 7	TTA Asn TCA AGT Ser 00 AAC	GAC CTG ASP AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
AAA TTT Lys GCT CGA Ala ATT	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6. ACT TGA Thr AGC TCG	AGT Ser 40 GCA CGT Ala 690 CAA GTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TTP	GAA Leu 650 AAT TTA ASD 7	TTA Asn TCA AGT Ser 00 AAC	GAC CTG ASP AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
AAA TTT Lys GCT CGA Ala ATT	TCT AGA Ser 630 ACT TGA Thr AGT TCA	AAA TIT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6. ACT TGA Thr AGC TCG	AGT Ser 40 • GCA CGT Ala 690 • CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TTP	GAA Leu 650 AAT TTA ASD 7	TTA Asn TCA AGT Ser 00 AAC	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 . ACT TGA Thr TCA Ser	AAA TIT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 6. ACT TGA Thr AGC TCG Ser	AGT Ser 40 • GCA CGT Ala 690 • CAA GTT Gln	GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp	GAA Leu 650 * AAT TTA ASD 7 AAA TTT Lys	TTA Asn TCA AGT Ser 00 AAC TTG Asn 750	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser 710 • TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 65 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA	AAA TIT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 6. ACT TGA Thr TGC TCG Ser GTA	AGT Ser  40  GCA CGT Ala  690  CAA GTT Gln	CAA Val  GCT CGA Ala  AAA TTT Lys  740  AAA	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 650 * AAT TTA ASD 7 AAA TTT Lys	TTA ASN TCA AGT Ser 00 AAC TTG ASN 750	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys CTA	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 . ACT TGA Thr TCA Ser ACA TGT	AAA TIT Lys 680 GTG CAC Val 7	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 6 ACT TGA Thr TCG Ser GTA CAT	AGT Ser  40  GCA CGT Ala  690  CAA GTT Gln	CAA Val	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 650 * AAT TTA ASD 7 AAA TTT Lys GAC	TTA ASN TCA AGT Ser 00 AAC TTG ASN 750 TCA AGT	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe TTC TGG	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys CTA GAT	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>

FIGURE 28 (2 of 3)

#### B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA
CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT
Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

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B-31 OSPA/ B-31 OSPB FUSION

20 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 80 70 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TIT\_TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 130 120 100 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 180 170 150 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 240 230 220 200 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 280 270 260 250 GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 330 320 310 300 290 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 380 370 360 350 AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TTT CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTA CTT Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 29 (1 of 3)

PCT/US94/12352

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B-31 OSP A/ B-31 OSP B FUSION

	390			40	0		4	10			420			43	0
AAA	GGT	GAA	• GTA	TCT	• Gaa	AAA	ATA	ATA	ACA	AGA	GCA	GAC	GGA	ACC	AGA
ጥጥ	CCA	CTT	CAT	AGA	CTT	TTT	TAT	TAT	TGT	TCT	CGT	CTG	CCT	TG3	TCT
Lys	Gly	Glu	Val	Ser	Glu	Lys	Ile	Ile	Thr	Arg	Ala	Asp	Gly	Thr	ÀſG>
	4	140			450			46	0	•	4	70			480
•		*		•	. ~		100	C 3 T	CCN	WC-T	CCN		CCT	222	CNC
CTT	GAA	TAC	ACA	GGA	TTA AAT	AAA maa	AGC	CTN	CCT	107	CCT	ALAL VOV	CCY	thi.	CTC
GAA	CTT	ATG	TGT	CLI	TIA	111	Ser	ASD	Ğlv	Ser	ด้าง	Lvs	Ala	Lvs	Glu>
Leu	GIU	lyr	Ini	GIY	116	Lys	361	nsp	013		,	_,_		-,-	
		49	90		5	00			510			52	20 .		
	•		•	•		•		•	•		•		•	•	
GTT	TTA	AAA	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
CAA	AAT	TTT	CCG	ATA	CAA	GAA	CTT	CCT	TGA	GAT	TGA	CGA	CTT	TTT	TGT
Val	Leu	Lys	Gly	Tyr	Val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
530			540			55	50		9	560			570		
•		•	•		•		•	•		•		•	•	•	•
ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT	TCA
TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	TAA	AGT
Thr	Leu	.Val	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Asn	Ile	Ser>
5	80			590			600			6	10		•	620	
		•		•		•	•		*		*	•		•	CCT .
AAA	TCT	GGG	GAA	• GTT	TCA	GTT	GAA	CTT	AAT	GAC	* ACT	GAC	AGT	AGT	GCT
AAA TTT	TCT AGA	CCC	GAA	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC	* ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TTT	TCT AGA	CCC	GAA	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC	* ACT TGA	CTG	AGT TCA	AGT TCA	GCT CGA Ala>
AAA TTT	TCT AGA	CCC	GAA	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC	* ACT TGA	CTG	AGT TCA	AGT TCA Ser	CGA
AAA TTT Lys	TCT AGA Ser	Gly	GAA CTT Glu	GTT CAA Val	AGT Ser 40	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TTT Lys	TCT AGA Ser 630	Gly	GAA CTT Glu	GTT CAA Val 6	AGT Ser 40 • GCA	CAA Val	GAA CTT Glu	GAA Leu 650 •	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660	ASP AGC	AGT TCA Ser	AGT TCA Ser 6	CGA Ala> 70 • ACA
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT	Gly AAA	GAA CTT Glu	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6' TTA AAT	CGA Ala> 70 ACA TGT
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT	Gly AAA	GAA CTT Glu	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6' TTA AAT	CGA Ala> 70 • ACA
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT	Gly AAA	GAA CTT Glu	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA Asn	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6' TTA AAT	CGA Ala> 70 ACA TGT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 • GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn	GAC CTG Asp	GAC CTG Asp : AGT : TCA	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTI Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 • GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD	GAC CTG Asp	GAC CTG Asp : AGT : TCA : TCA	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6' TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	GAC CTG Asp : AGT : TCA : Ser	ACT TGA Thr 660 ACT TGA Thr CGA CCAC	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6' TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	GAC CTG Asp : AGT : TCA : Ser	ACT TGA Thr 660 ACT TGA Thr CGA CCAC	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6' TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTI Lys 680 CCA CGA	GAA CTT AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7	GAC CTG Asp	GAC CTG ASP AGT TCA Ser TTCA AAC Let	ACT TGA Thr 660 ACT TGA Thr CGA CCAC	AGC TCG Ser 710 TTCC AAGC	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6' TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 GCA CGA	GAA CTT Glu AAA TTT GLys GAC A CTC A Asp	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 • GCA CGT Ala 690 • AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD 7 AAA TTI Lys	GAC CTG Asp 00 GAT CTA Asp	GAC CTG ASP AGT TCA AAC AAC Let	ACT TGA Thr 660 ACT TGA TGA TCA TCA TCA CCA CCA CCA CCA CCA CCA CC	AGC TCG Ser 710 AGC TTG	AGT TCA Ser ACT TGA Thr TTA AAT Leu	AGT TCA Ser ETTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>
AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 GCA CGA	GAA CTT GAC	GTT CAA Val  6 ACT TGA Thr AGC TCG	AGT Ser 40 • GCA CGT Ala 690 • AAA TTT Lys	CAA Val  GCT CGA Ala  AAA TTT Lys 740 . CAA	GAA CIT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7 AAA TTI Lys	GAC	GAC CTG ASP AGT TCA AAC AAC AAC AAC AAC AAC AAC AAC AA	ACT TGA Thr 660 ACT TGA TGA TCA TCA CCAC	AGC TCG Ser 710 AGC AGC AGC AGC AGC AGC	AGT TCA Ser ACT TGA Thr TGA Thr 60	AGT TCA Ser  E TTA AAT Leu ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 CGA CGA A AT	GAA CTT GAC ACTO ACTO ACTO ACTO ACTO ACTO ACTO AC	GTT CAA Val  6 ACT TGA Thr AGC TCG Ser	AGT Ser  40  GCA CGT Ala  690  AAA TTT Lys	CAA Va1  GCT CGA Ala  AAA TTT Lys  740  CAA GTT	GAA CIT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 650 AAT TTA Asn 7 AAA TTI Lys	GAC	GAC CTG ASP AGT TCA AAC D Let A GCT	ACT TGA Thr 660 ACT TGA TGA TCA TCA CCA CCA CCA CCA CCA CCA CCA CC	AGC TCG Ser 710 AGC AGC TTCG AGC TTCG TTCG TTCG TTCG	AGT TCA Ser ACT TGA Thr TGA Thr GA AAA Thr GA AAA AAA GA AAA AAAA	AGT TCA Ser  E TTA AAT Leu ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>

FIGURE 29 (2 of 3)

B-31 OSP A/ B-31 OSP B FUSION

770 780 790 800 810

GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT TTA
CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA AAT
Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

#### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

nce Range: 1 to 1401

30 20 10 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 80 70 60 50 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA-AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 130 120 110 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 180 170 160 150 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 230 220 210 200 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 280 270 260 250 GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 330 320 310 300 290 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 370 360 350 340 AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TTT CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTA CTT Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 30 (1 of 4)

60//33

## B-31 OAP A/ B-31 OSP B / B-31 OSPC FUSION

		400		A 1	10			420			43	<u> </u>
390	_	400		•	•		•	•		•		•
AAA GGT GAA		~~ ~\		አጥል :	ልጥል	ACA	AGA	GCA	GAC	GGA	ACC	AGA
AAA GGT GAA TTT CCA CTT	GTA T	CT GAA	ሌሌሌ የሌሌ	TAT '	TAT	TGT	TCT	CGT	CTG	CCT	TGG	TCT
Lys Gly Glu	CAT A	GA CII	111	Tla	Tle	Thr	Ara	Ala	Asp	Gly	Thr	Arg>
Lys Gly Glu	Val S	er Giu	Lys	110			5		•	•		
		450		•	46	60		4	70			480
440		450		•	3.	•	•		•		•	•
CTT GAA TAG			888	»CC	CAT	GGA	TCT	GGA	AAA	GCT	AAA	GλG
CTT GAA TAC	ACA G	GA ATT	WWW.	TCG	CTA	CĊT	AGA:	CCT	TTT	CGA	TTT	CIC
GAA CTT ATO	TGT C	CT TAA	111	Cor	350	Clv	Ser	Glv	Lvs	Ala	Lys	Glu>
Leu Glu Ty	c Thr C	31A 116	Lys	261	vəħ	023		,	-, -	•	•	
			500			510			5:	20		
	490		•		•	•		•		•	•	
GTT TTA AA		ጉእጥ ርጥጥ -	СТТ	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
_			-c	L-1-1.	1.0	100	uni	100	COA	~		
CAA AAT TT Val Leu Ly	T CCG 4	MIM CAA	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
Val Leu Ly	2 CIA	IYI VAL	Dea		,							
	540		5	50			560			570		
530	_	•	_	•	•		•		•	•		•
ACA TTG GT	C CTT	AAA GAA	GGA	ACT	GTI	ACT	TT	AGC	AAA	. AAT	TTA	TCA
			י ככי	' TGA	CAA	1 167	/ WW1	100				1102
TGT AAC CA	1 Val	Lys Glu	Gly	Thr	Va]	Thi	Lei	ı Ser	Lys	Asn	Ile	Ser>
Thi bed ve			_									
580	5	90		600			(	510			620	
580	_		•	•		•		•	•		•	
•	•	+ 	• A GTT	440.7		• 'AA 1	r GA	· C ACT	GAO	AG7	AG7	CCT
AAA TCT GO	G GAA	GTT TC	T ( T )	GAA	CT	A 114	r ga	ACI G TGA	, ,,,,	3 1-7	AG7	
AAA TCT GO	G GAA	GTT TC	T ( T )	GAA	CT	A 114	r ga	ACI G TGA	, ,,,,	3 1-7	AG7	
•	G GAA	GTT TCA CAA AG Val Se	T ( T )	GAA	CT: GA: Le	u As:	r ga	E ACT G TG/ p Thi	. Ası	3 1-7	AGT A TCA	Ala>
AAA TCT GO	G GAA	GTT TC	T ( T )	GAA	CT	u As:	r ga	ACI G TGA	. Ası	3 1-7	AGT A TCA	
AAA TCT GC TTT AGA CC Lys Ser G	GG GAA	GTT TCZ CAA AG' Val Se:	r Vai	GAA A CTI l Glu	CT GA Le	u As:	r GA( A CT) n As;	ACT G TG/ p Thi	Ası	o Sei	A TCA	70
AAA TCT GC TTT AGA CC Lys Ser G	GG GAA	GTT TCZ CAA AG' Val Se:	r CA	GAA A CTT 1 Glu	CTT GALL	u As:	T GA( A CT) A As	ACT ACT	r Ası	Sei	A TCA	: Ala> 570 A ACA
AAA TCT GC TTT AGA CC Lys Ser G	GG GAA CC CTT ly Glu	GTT TC: CAA AG' Val Se: 640	r CA r Va:	r GAA A CTT l Glu	CTT GALLER GEORGE	u As:	T GA( A CT( A AS)	T AC	ASI T AGA	Sei	T AGTA TCA	A ACA
AAA TCT GC TTT AGA CC Lys Ser G	GG GAA CC CTT ly Glu	GTT TC: CAA AG' Val Se: 640	r CA r Va:	r GAA A CTT l Glu	CTT GALLER GEORGE	u As:	T GA( A CT( A AS)	T AC	ASI T AGA	Sei	T AGTA TCA	A ACA
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu AA AAA TT TTT ys Lys	GTT TCA CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	r CA r Va: A GC T CG a Al	r GAA A CTT l Glu	CTT GALLER GEORGE	T GA	T GA( A CT( A AS)	T AC	ASI T AGA T TC	C ACG TG.	T AGTA TCA	A ACA
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu AA AAA TT TTT ys Lys	GTT TC/CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	r CAI r Vai A GC T CG a Al	r GAA A CTT l Glu T TGC A ACC a Tr	GAAC TT	T GA	T GAM	C ACT G TGA P Thu 660 T ACT A TG. Ex Th	r Asi	C AC G TG	T AGT A TCA T Ser T TTA A AA' r Le	Ala> ACA T TGT U Thr>
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu AA AAA TT TTT ys Lys	GTT TC/CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	r CAI	T TGCA ACCA TI	G AA	T GA	T GAI A CTI A AS C AG G TC P Se	C ACT G TGA P Thi 660 T ACT A TGA ET Th	r Asi	C ACG TG.	T AGT A TCA T Ser T TTA A AA' T Le	Ala>  AACA T TGT Thr>  720 TA GAT
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu  AA AAA TT TTT ys Lys	GTT TC/CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	r CA r Va: A GC T CG a Al	T TGO A ACC A TT	GAAC TT AA	T GA	T GAG A CTG A ASS C AG C AG C AG C AG T TC	C ACT G TGA P Thi 660 T AC TA TG ET Th	T AGE T AGE T TO T T	C AC Th	T AGT T TCA T TTA A AA' T Le	A ACA T TGT Thr> 720 TA GAT TGT CTA
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu  AA AAA TT TTT ys Lys	GTT TC/CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	r CA r Va: A GC T CG a Al	T TGO A ACC A TT	GAAC TT AA	T GA	T GAG A CTG A ASS C AG C AG C AG C AG T TC	C ACT G TGA P Thi 660 T AC TA TG ET Th	T AGE T AGE T TO T T	C AC Th	T AGT T TCA T TTA A AA' T Le	A ACA T TGT Thr> 720 TA GAT TGT CTA
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu  AA AAA TT TTT ys Lys	GTT TC/CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	r CA r Va: A GC T CG a Al	T TGO A ACC A TT	GAAC TT AA	T GA	T GAG A CTG A ASS C AG C AG C AG C AG T TC	C ACT G TGA P Thi 660 T AC TA TG ET Th	T AGE T AGE T TO T T	C AC Th	T AGT T TCA T TTA A AA' T Le	A ACA T TGT Thr> 720 TA GAT TGT CTA
AAA TCT GG TTT AGA CG Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L	GG GAA CC CTT ly Glu  AA AAA TT TTT ys Lys CC GAC CGA CTG	GTT TC/CAA AG' Val Se: 640 ACT GC TGA CG Thr Al	T CAN T Va.  A GC T CG A A1 O AAA AA TT TI ys Ly	T TGC A ACC A TT	GAAC TT AA	T GA TA CT	T GAG A CTG A ASS C AG C AG C AG C AG T TC	C ACT G TGA P Thi 660 T AC TA TG ET Th	T AGE T AGE T TO T T	C AC Th	T AGT T TCA T TTA A AA' T Le	A ACA T TGT Thr> 720 TA GAT TGT CTA
AAA TCT GC TTT AGA CC Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L  68  ATT AGT C TAA TCA C Ile Ser A	AA AAA TT TTT YS LYS CGA CTG A1a ASE	GTT TC: CAA AG' Val Se: 640 ACT GC TGA CG Thr Al 69 AGC AA TCG TI Ser Ly	A GC T CG A Al	T TGCA ACCA A CTT	GAN CONTRACTOR ASSESSED TO ASS	T GA	C AG TO Se AT TA AA ASS L	C ACT G TGA P Thu 660 T ACT A TG T Th TG GT AC CA eu Va	T AGA TC	C AC G TG T Th	T AGTA TOP	A ACA T TGT Thr> 720 TA GAT TT CTA TASP>
AAA TCT GC TTT AGA CC Lys Ser G  630 GCT ACT A CGA TGA T Ala Thr L  68 ATT AGT C TAA TCA C Ile Ser J	AA AAA TT TTT YS LYS CGA CTG Ala ASF	GTT TCX CAA AG Val Se: 640 ACT GC TGA CG Thr Al 69 AGC AA TCG TY Ser Ly	A GC A A A A A A A A A A A A A A A A A A	T TGC A ACC A TT A ACC T TG T	CT GAN Lee	T GA	C AG TO See L	C ACT	T AGE T AGE T TO T T	C AC TING AM TO	T AGTA TOA	A ACA T TGT Thr> 720 TA GAT TT CTA T ASP>
AAA TCT GC TTT AGA CC Lys Ser G  630 GCT ACT A CGA TGA T Ala Thr L  68 ATT AGT C TAA TCA C Ile Ser J	AA AAA TT TTT YS LYS CGA CTG Ala ASP	GTT TCX CAA AG Val Se: 640 ACT GC TGA CG Thr Al 69 AGT ACT TCG TX Ser Ly	A GC A AA AA CA	T TGC A ACC T TG A ACC T TG T	CT' GA C GA 650 650 G AA C TT P AS T AI AC A	T GAA CT	C AG CC	C ACT G TGA C TAC C A TG C TAC C CA C C CA C C C C C C C C C C C C C	T AGO T AGO T TO T	C AC TING AM TO AC	T AGTA TOP	A ACA T TGT Thr> 720 TA GAT TT CTA T ASP> TA GAA AT CTT
AAA TCT GC TTT AGA CC Lys Ser G  630  GCT ACT A CGA TGA T Ala Thr L  68  ATT AGT C TAA TCA C Ile Ser A	AA AAA TT TTT YS LYS CGA CTG Ala ASP	GTT TCX CAA AG Val Se: 640 ACT GC TGA CG Thr Al 69 AGT ACT TCG TX Ser Ly	A GC A AA AA CA	T TGC A ACC T TG A ACC T TG T	CT' GA C GA 650 650 G AA C TT P AS T AI AC A	T GAA CT	C AG CC	C ACT G TGA C TAC C A TG C TAC C CA C C CA C C C C C C C C C C C C C	T AGO T AGO T TO T	C AC TING AM TO AC	T AGTA TOP	A ACA T TGT Thr> 720 TA GAT TT CTA T ASP> TA GAA AT CTT

FIGURE 30 (2 of 4)

#### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

7	70			780			79	0		8	300			810		
	•		•	•		•		•	•		•		•	•		•
					GAA											
					CTT											
	Gly	Ser	Ala	Ser	Glu	Ile	Lys	Asn	Leu	Ser	Glu	Leu	Lys	ÀS	Ala	Leu>
	82	0		8	30			840			85	0		9	50	
		•	•		•		•	•		•		•	•		•	
					AAT											
					TTA											
	Lys	Met	Ala	Asn	Asn	Ser	Gly	Lys	Asp	GIA	ASD.	Thr	Ser	Ala	ASΠ	Ser>
		870			88	30		8	90			900			91	. ο
	•	•		•		•	•		•		•	•		•		•
					GTT											
					CAA											
	Ala	Asp	Glu	Ser	Val	Lys	Gly	Pro	ASD	ren	Thr	GIU	iie	Ser	Lys	Lys>
		. 9	920			930			94	10		9	50			960
	•		•	•	•	•		*		•	*		•		•	•
					AAT											
					TTA											
	Ile	Thr	Asp	Ser	Asn	ΑΙΞ	vaı	Leu	Leu	ATG	vaı	Lys	GIU	Val	Glu	Ala>
			9.	70		!	980			990			100	00		
		•		•	•		•		•	•		•		•	•	
					ATA											
					TAT											Lys>
	Leu	ren	ser	Ser	116	жър	GIU	116	MIG	VIG		WIG	116	GIA	Lys	LŽZ>
1(	10			1020			10	30		1	040		:	1050		
	*		•	•		•		*	•		•		•	*		•
					AAT											
					TTA											
	116	HIS	GIN	ASn	ASN	GIA	Leu	ASP	ini	GIU	ıyı	ASI	HIS	ASN	GIA	Ser>
	30	<b>C O</b>		1	070			1080			10	90		1:	100	
	10	00														
		•			•		•	•		•		•	•		•	
	TTG	• TTA		GGA	CGT											
	TTG AAC	TTA	CGC	GGA CCT	GCA	ATA	CGT	TAT	AGT	TGG	GAT	TAT	TTT	GTT	TTT	TAA
	TTG AAC	TTA	CGC	GGA CCT	GCA	ATA	CGT	TAT	AGT	TGG	GAT	TAT	TTT	GTT	TTT	
	TTG AAC Leu	TTA	CGC	GGA CCT	GCA	ATA Tyr	CGT	TAT	AGT	TGG	GAT Leu	TAT	TTT	GTT	TTT	AAT Leu>
	TTG AAC Leu	TTA AAT Leu	CGC	GGA CCT	GCA Arg	ATA Tyr	CGT	TAT	AGT Ser	TGG	GAT Leu	TAT Ile	TTT	GTT	TTT Lys	AAT Leu>
	TTG AAC Leu	TTA AAT Leu 1110 GGA	CGC Ala	GGA CCT Gly	GCA Arg 11 AAT	ATA Tyr 20 • GAA	CGT Ala	TAT Ile  1 TTA	AGT Ser 130	TGG Thr	GAT Leu	TAT Ile 1140 ATT	TTT Lys GAT	GTT Gln GCG	TTT Lys 115	AAT Leu>
	TTG AAC Leu  GAT CTA	TTA AAT Leu 1110 GGA CCT	CGC Ala	GGA CCT Gly	GCA Arg 11 AAT TTA	ATA Tyr 20 GAA CTT	CGT Ala	TAT Ile  1 TTA AAT	AGT Ser 130 AAG	TGG Thr GAA	GAT Leu	TAT Ile 1140 ATT TAA	TTT Lys GAT CTA	GTT Gln GCG CGC	TTT Lys 11: GCT CGA	AAT Leu>

FIGURE 30 (3 of 4)

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### B-31 OSP A / B-31 OSP B/ B-31 OSP C FUSION

1190 1180 1170 1160 AAA TGT TCT GAA ACA TTT ACT AAT AAA TTA AAA GCA AAA CAC ACA GAT TTT ACA AGA CTT TGT AAA TGA TTA TTT AAT TTT CGT TTT GTG TGT CTA Lys Cys Ser Glu Thr Phe Thr Asn Lys Leu Lys Ala Lys His Thr Asp> 1240 1230 1220 1210 CTT GGT AAA GAA GGT GTT ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA GAA CCA TTT CTT CCA CAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT Leu Gly Lys Glu Gly Val Thr Asp Ala Asp Ala Lys Glu Ala Ile Leu> 1290 1280 1270 1260 1250 • AAA ACA AAT GGT ACT AAA ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT TGT TTA CCA TGA TTT TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT Lys Thr Asn Gly Thr Lys Thr Lys Gly Ala Glu Glu Leu Gly Lys Leu> 1320 1330 1310 TTT GAA TCA GTA GAG GTC TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAA CTT AGT CAT CTC CAG AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA Phe Glu Ser Val Glu Val Leu Ser Lys Ala Ala Lys Glu Met Leu Ala> 1380 1370 1360 1350 • . AAT TCA GTT AAA GAG CTT ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA TTA AGT CAA TTT CTC GAA TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser Pro Lys>

1400

AAA CCT TAA TTT GGA ATT Lys Pro \*\*\*>

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#### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

		1	.0			20			30			4	0		
	•		•	•		•		•	•		•		•	•	
ATG	AAA	AAG	AAT	ACA	TTA	AGT	GCG	ATA	TTA	ATG	ACT	TTA	TTT	TTA	TTT
TAC	TTT	TTC	TTA	TGT	TAA	TCA	CGC	TAT	AAT	TAC	TGA	AAT	AAA	TÁK	AAA
Met	Lys	Lys	Asn	Thr	Leu	Ser	Ala	Ile	Leu	Met	Thr	Leu	Phe	Leu	Phe>
	-	-							•						
50			60			7	70			80			90		
•		•	•		•		•	•		•		•	•		•
ATA	TCT	TGT	AAT	TAA	TCA	GGG	AAA	GAT	GGG	AAT	ACA	TCT	GCA	TAK	TCT
TAT	AGA	ACA	TTA	ATT	AGT	CCC	TTT	CTA	CGC	TTA-	TGT	AGA	CGT	TTA	AGA
Ile	Ser	Cys	Asn	Asn	Ser	Gly	Lys	Asp	Gly	Asn	Thr	Ser	Ala	Asn	Ser>
10	00		3	110		_	120		_	13	50	_	3	140	
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				GTT											
				CAA											
Ala	Asp	GIU	Ser	vaı	Lys	GIA	PIO	WPII	Leu	1111	Giu	116	261	∴y S	Lys>
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•	130		•	- `	•	•		•		•	•		•	-	•
ATT	ACG	GAT	TCT	AAT	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG
TAA	TGC	CTA	AGA	TTA	CGC	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAA	CTT	CGC
Ile	Thr	Asp	Ser	Asn	Ala	Val	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala>
		200			210			2:	20			230			245
•		•		• .	•		•		•	•		•		•	•
TTG	CTG	TCA	TCT	ATA	GAT	GAA	ATT	GCT	GCT	AAA	GCT	ATT	GGT	AAA	<del>አ</del> ኢት
AAC	GAC	AGT	AGA	TAT	CTA	CTT	TAA	CGA	CGA	TTT	CGA	TAA	CCA	TTT	TTT
Leu	Leu	Ser	Ser	Ile	Asp	Glu	Ile	Ala	Ala	Lys	Ala	He	Gly	Lys	Lys>
		_				200			270			2	80		
		2	50		•	260		•	270			2	•		
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### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

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AAA T	TOT	TCT	GAA	ACA	lil	ACT	TAA	AAA	TTA	AAA TTT	CGT	AAA TTT	CAC	TCT	CYI
TTT A	ICA	AGA	CIT	Thr	AAA Pho	Thr	JIM	ive	ren	Lvs	Ala	Lvs	His	Thr	ÀSD>
Lys C	.ys	Ser	GIU	1111	PHE	1111	N3!!	Lys	<i>D</i> . u	_, _					
	4	40			450			46	0		4	70			480
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CTT	GT	AAA	ĠAA	GGT	GTT	ACT	GAT	GCT	GAT	GCA	AAA	GAA	GCC	TTA	TTA
GAA (	CA	TTT	CTT	CCA	CAA	TGA	CTA	CGA	CTA	CGT	TTT	CTT	CGG	TAA	AAT • • • • • • • • • • • • • • • • • • •
Leu (	Sly	Lys	Glu	Gly	Val	Thr	Asp	Ala	ASP	ATS	Lys	GIU	ATG	116	_eu>
		40	90			00			510			52	20		
	•	4:	•	•	•	•		•	•		•		•	•	
AAA 2	ACA	AAT	GGT	ACT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	CTT	GGA	ልልል	TTA
TTT T	TGT	TTA	CCA	TGA	TTT	TGA	TTT	CCA	CGA	CTT	CTT	GAA	CCT	TTT	AAT
Ĺys '	Thr	Asn	Gly	Thr	Lys	Thr	Lys	Gly	Ala	Glu	Glu	Leu	Gly	Lys	Leu>
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530	•		540			5:	50		-	60		•	570		•
TTT	C	TCA	CT3	GAG	GTC	ттс	TCA	AAA	GCA	GCT	AAA	GAG	ATG	CTT	GCT
AAA	ርጥጥ	) CT	CAT	CTC	CAG	AAC	AGT	TTT	CGT	CGA	TTT	CTC	TAC	GAA	CGA
Phe	Glu	Ser	Val	Glu	Val	Leu	Ser	Lys	Ala	Ala	Lys	Glu	Met	Leu	Ala>
58	0			590			600		_	6	10		(	520	
	•	•		GAG	CWW	* *C	200	CCT	ىلىدات م	CTC	GCA	GA A	AGT	CCA	22A
AAT	TCA	GII	AAA	CTC	CII	TOT	TCG	CCI	CAA	CAC	CGT	CTT	TCA	GGT	TTT
) TIM	SOT	Val	LVS	Glu	Leu	Thr	Ser	Pro	Val	Val	Ala	Glu	Ser	Pro	Lys>
no.			, _												
	630			6	40			650			660			67	70
•	•		•		*	*		•		•	•		*	~~~	TC)
AAA	CCT	AAC	CAA	AAT	GTT	AGC	AGC	CTT	GAC	GAG	AAA	AAC	AGC	CAA	ACT
TTT	GGA	TTC	GTI	TTA	CAA	TCG	Ser	GAA	Acn	Glu	TVS	Asn	Ser	Val	Ser>
Lys	Pro	, rås	GII	ı ASII	vai	261	261	Deu	, nop	0.0					
		680			690			7	00			710			720
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GTA	GAT	TT	CCI	GGI	GAA	OTA	AAA :	GTI	CTI	GTA	AGC	: AAA	GAA	AAA	AAC
CAT	CT	AA /	C GG?	CCA	CTI	TAC	TTI	CA	GAA	CAT	TCG	TII	CTI	TIT	TTG
Val	Ası	) Le	ı Pro	o Gly	Glu	Met	Lys	val	l Leu	ı Vai	Ser	. rAs	GIU	Lys	Asn>
			730			740			750	)		7	60		
						. 40		•		•	•	•	•	•	
AAA	GA	G GG	C AA	S TAC	GAT	CT	A AT	r GC	A ACA	A GT	A GAC	AAC	CTI	GAG	CII
TTT	CT(	s cc	G TT	TA D	G CT	A GA	KAT 1	A CG	r TG7	CA!	r cro	TTC	: GA	CTC	GAA
Lys	Ası	p <b>G1</b>	y Ly	s Ту	r Ası	) Le	ı Ile	e Ala	a Thi	va:	l Ası	) Lys	Lei	Glu	Leu
					FI	.GURE	<b>,31</b>	(2 0	f 4)					e)	

PCT/US94/12352

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### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

			780			79	ο.		8	300			810		
770			•		•	_	•	•		•		•	•		•
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		~~ `	203	CT)	there	ጥፐር	TTA	CCT	AGA	CCI	CW1		C11	ccc	CV1
TIT	CCT	1GA	Non	Acn	Ivs	Asn	Asn	Glv	Ser	Gly	Val	Leu	Glu	Gly	Val>
Lys	CTA	1111	361	Vab	<i>D</i> <sub>3</sub> <i>D</i>					_					
0.	30		,	830			840			85	50		8	360	
82	_			*		•	•		*		•	•		•	
	-	GAC		AGT	AAA	GTA	AAA	TTA	ACA	ATT	TCT	GAC	GAT	CTA	GGT
		~	- The state of	$a \sim a$	TATE	$C\lambda T$	TTT	AAT	TGT	TAA	AGA	CIG	CIA	CWT	CCA
111	Ala	yen	Lvs	Ser	Lvs	Val	Lys	Leu	Thr	Ile	Ser	Asp	Asp	Leu	Gly>
Lys	VIG	AJP	,_				_								
	870			8	во		1	890			900			9	10
•			•		•	•		•		•	•		•		•
CAA	ACC	ACA	CTT	GAA	GTT	TTC	AAA	GAA	GAT	GGC	AAA	ACA	CTA	GTA	TCA
		m-0-1		CTT	CVV	AAC	TTT	CTT	CTA	CCG	1-1-1	161	GAI	Cr.	WOI
Gln	Thr	Thi	Leu	Glu	Val	Phe	Lys	Glu	Asp	Gly	Lys	Thr	Leu	Val	Ser>
01															
		920			930			9	40			950			960
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AAA	. AAJ	GT	A ACT	TCC	AAA :	GAC	AAG	TCA	TC	ACA	GAA	GAA	AAA	TTC	AAT
			n m^ 1	NCC	thurth.	· (~TC	TTC	AGT	` AG1	161	CII	CII	1.11	AAA G	LIN
Lys	Lys	Va!	1 Thi	Ser	Lys	Asp	Lys	Ser	Sei	Thr	GIU	GIU	Lys	Pne	Asn>
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			970			980		_	990	,		10	•		,
	•		•		, 	•			እምነ		) ACA	CCA	GAC	· cc:	ACC
GAZ	AA A	A GG	T GA	A GT	TC	GAF		r wys	ימידי ז ימידי ז	ה שלכם ה	י אטא דייריי	י רכז	CTO	CC:	ACC TGG
CTI	TT	r cc	A CT	r CA	r AGA	. 61.	. 111	. IN.	. IN	Th:	. Ard	Ala	Ast	Glv	TGG Thr>
Gli	ı Ly	s Gl	A CI	u va.	r Sei	GIL	ı Ly:	, TT.	- 11				,		
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AL	g Le	U G2				,									
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GA	G GT	T T	ta aj	A GG	C TA	T GT	T CT	T GA	A GC	A AC	T CT	A AC	T GC	T GA	ጸ ጸጸጸ ፕ ፕፕፕ
				~ ~	CAT	מה מי	A GA	A CT	T CO	T TG	A GA	T TG	A CG	A CI	7 777
G1	u Va	al L	eu Ly	rs G1	у Ту	r Va	1 Le	u Gl	u G	y Th	r Le	u Th	r Al	a Gl	u Lys>
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AC	CA AC	CA T	TG G	TG G7	t a	AA GA	LA GO	SA AC	CT G	TT AC	T TI	A AC	C AF	<b>LA Α</b> Δ	TTA TA
TT/	~~ ~	CT 3	3C C	AC C	T A	rr Ci	רד כנ	CT TO	GA C	NA TO	SA AA	T TC	.G 17	(T. T.)	W IVV
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FIGURE 31 (3 of 4)

B-31 OSP C/ B-31 OSP A / B-31 OSP B FUSION

1160 1170 1180 1190 1200 TCA AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT AGT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA Ser Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser> 1220 1230 GCT GCT ACT AAA AAA ACT GCA GCT TGG AAT GAC AGT ACT AGC ACT TTA CGA CGA TGA TTT TTT TGA CGT CGA ACC TTA CTG TCA TGA TCG TGA AAT Ala Ala Thr Lys Lys Thr Ala Ala Trp Asn Asp Ser Thr Ser Thr Leu> 1250 1260 1270 ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA GAT TTG GTG TTC TTA ACA TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT CTA AAC CAC AAG AAT TGT Thr Ile Ser Ala Asp Ser Lys Lys Thr Lys Asp Leu Val Phe Leu Thr> 1300 1310 1320 1330 GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC ACA GCT GGA ACC AGC CTA CTA CCA TGT TAA TGT CAT GTT GTT ATG TTG TGT CGA CCT TGG TCG GAT Asp Gly Thr Ile Thr Val Gln Gln Tyr Asn Thr Ala Gly Thr Ser Leu> 1360 1370 1380 GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala>

1400

TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

#### **FUSION SEQUENCE**

B-31 OSP A/ B-31 P-93 (1168-2100)
Sequence Range: 1 to 1720

10 . 20 30 • AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA GAT TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT CTA K Q N V S S L D E K N S V S V D> 50 60 70 . 80\_\_\_. TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA GAC AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT CTG L P G E M K V L V S K E K N K D> 120 130 110 GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA GGA CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT CCT G K Y D L I A T V D K L E L K G> 170 150 160 180 ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA GCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT CGA T S D K N N G S G V L E G V K A> 210 200 220 230 GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA ACC CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT TGG D K S K V K L T I S D D L G Q T> 260 270 250 280 ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA AAA TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT TTT T L E V F K E D G K T L V S K K> 300 310 320 330 GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA AAA CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTA CTT TTT V T S K D K S S T E E K F N E K> 370 350 360 GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GAC GGA ACC AGA CTT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT GAA G E V S E K I I T R A D G T R L>

FIGURE 32 (1 of 5)

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WO 95/12676

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B-31 OSP A/ B-31 P93

	390			40	00		4	110			420			4:	30
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					AAA TTT										
E	Y10	T	G	I	к	s	D	G.		G	ĸ	A	ĸ	E	V>
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	4	440		_	450			46	50	_	4	170			480
TTA	AAA	GGC	ТАТ	- GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	444	) )	ACA
					GAA										
L	K	G	Y	v	L	E	G	T			. A.		ĸ	T	T>
		4	90			500			510			5:	20		
	•	-	•	•	•	*		•	•		•	٠.	•	•	
					GGA										
		CAA			CCT	TGA T	CAA								
L	V	٧	K	E	G	1	V	T	L	S	K	N	I	S	K>
530			540			55	50			560			570		
* *		<b>C</b>	•	mc >	-	C	•	• 33m	~ ~	•	~~~	•	•		•
					GTT CAA										
s		· E	v	s	v		L	N			D	s	s	A	λ>
51	80	•	!	590		•	600		•	61	10	•	(	520	
	•	• AAA		•	GCT	• TGG	•	TCA	• GGC		•	ACT		•	ATT
ACT TGA	AAA TTT	TTT	ACT TGA	GCA CGT	GCT CGA	ACC	AAT TTA	AGT	CCG	ACT	• TCA		TTA	ACA	
ACT	AAA		ACT	• GCA			• Taa			ACT	• TCA		TTA	ACA	
ACT TGA	AAA TTT	TTT	ACT TGA	GCA CGT A	CGA	ACC	AAT TTA N	AGT	CCG	ACT TGA	TCA AGT	TGA	TTA AAT	ACA TGT	TAA I>
ACT TGA T	AAA TTT K 630	TTT	ACT TGA T	GCA CGT A	CGA A	ACC W	AAT TTA N	AGT S S 50	CCG G	ACT TGA T	TCA AGT S	TGA T	TTA AAT L	ACA TGT T	TAA I> 70
ACT TGA T	AAA TTT K 630 GTA	TTT K	ACT TGA T	GCA CGT A	CGA A 40 AAA	ACC W	AAT TTA N	AGT S 550 GAC	CCG G	ACT TGA T	TCA AGT S 660	TGA T	TTA AAT L AAA	ACA TGT T	TAA I> 70 AAC
ACT TGA T • ACT TGA	AAA TTT K 630 GTA CAT	TTT K AAC TTG	ACT TGA T * AGT TCA	GCA CGT A 64 AAA TTT	CGA A 10 AAA TTT	ACC W ACT TGA	AAT TTA N AAA TTT	AGT S 50 GAC CTG	CCG G CTT GAA	ACT TGA T • GTG CAC	TCA AGT S 660 TTT AAA	TGA T ACA TGT	TTA AAT L AAA TTT	ACA TGT T 67 GAA CTT	TAA I> 70 • AAC TTG
ACT TGA T	AAA TTT K 630 GTA	TTT K	ACT TGA T	GCA CGT A	CGA A 40 AAA	ACC W	AAT TTA N	AGT S 550 GAC	CCG G	ACT TGA T	TCA AGT S 660	TGA T	TTA AAT L AAA	ACA TGT T	TAA I> 70 AAC
ACT TGA T • ACT TGA	AAA TTT K 630 GTA CAT V	TTT K AAC TTG	ACT TGA T * AGT TCA	GCA CGT A 64 AAA TTT	CGA A 10 AAA TTT	ACC W ACT TGA	AAT TTA N AAA TTT	AGT S 550 GAC CTG D	CCG G CTT GAA	ACT TGA T • GTG CAC	TCA AGT S 660 TTT AAA F	TGA T ACA TGT	TTA AAT L AAA TTT	ACA TGT T 67 GAA CTT	TAA I> 70 • AAC TTG
ACT TGA T ACT TGA T	AAA TTT K 630 GTA CAT V	AAC TTG N	ACT TGA T * AGT TCA S	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690	ACC W ACT TGA T	AAT TTA N AAA TTT K	AGT S 650 GAC CTG D	CCG G CTT GAA L	ACT TGA T • GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L AAA TTT K	ACA TGT T 67 GAA CTT E	TAA I> 70 AAC TTG N> 720
ACT TGA T ACT TGA T	AAA TTT K 630 GTA CAT V	AAC TTG N 680	ACT TGA T AGT TCA S	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690	ACC W ACT TGA T	AAT TTA N AAA TTT K	AGT S 650 GAC CTG D 70	CCG G CTT GAA L	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L AAA TTT K	ACA TGT T 67 GAA CTT E	TAA I> 70 AAC TTG N> 720 GGG
ACT TGA T ACT TGA T	AAA TTT K 630 GTA CAT V	AAC TTG N 680	ACT TGA T AGT TCA S	GCA CGT A 64 AAA TTT K	CGA A 10 AAA TTT K 690	ACC W ACT TGA T TAC ATG	AAT TTA N AAA TTT K GAC CTG	AGT S 650 GAC CTG D 70	CCG G CTT GAA L	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T	TTA AAT L AAA TTT K	ACA TGT T 67 GAA CTT E	TAA I> 70 AAC TTG N> 720 GGG
ACT TGA T ACT TGA T ACA T ACA	AAA TTT K 630 GTA CAT V	AAC TTG N 680 ACA TGT T	ACT TGA T AGT TCA S GTA CAT V	GCA CGT A 64 AAA TTT K	CGA A A A A TTT K 690 CAA GTT Q	ACC W ACT TGA T TAC ATG Y	AAT TTA N AAA TTT K GAC CTG	AGT S 650 GAC CTG D 70 TCA AGT	CCG G CTT GAA L DO AAT TTA N	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T AAA TTT K	TTA AAT L AAA TTT K TTA AAT L	ACA TGT T 67 GAA CTT E GAG CTC	TAA I> 70 AAC TTG N> 720 GGG CCC
ACT TGA T ACT TGA T ACA T ACA	AAA TTT K 630 GTA CAT V	AAC TTG N 680 ACA TGT T	ACT TGA T AGT TCA S	GCA CGT A 64 AAA TTT K	CGA A A A A TTT K 690 CAA GTT Q	ACC W ACT TGA T TAC ATG	AAT TTA N AAA TTT K GAC CTG	AGT S 650 GAC CTG D 70 TCA AGT	CCG G CTT GAA L	ACT TGA T GTG CAC V	TCA AGT S 660 TTT AAA F	TGA T ACA TGT T AAA TTT K	TTA AAT L AAA TTT K	ACA TGT T 67 GAA CTT E GAG CTC	TAA I> 70 AAC TTG N> 720 GGG CCC
ACT TGA T ACT TGA T TGA T TCA	AAA TTT K 630 GTA CAT V ATT TAA I	AAC TTG N 680 ACA TGT T 7	ACT TGA T AGT TCA S GTA CAT V	GCA CGT A 64 AAA TTT K CAA GTT Q	CGA A 10 AAA TTT K 690 CAA GTT Q	ACC W ACT TGA T TAC ATG Y 740	AAT TTA N AAA TTT K GAC CTG D CTT	AGT S GAC CTG D TCA AGT S	CCG G GAA L DOO. AAT TTA N	ACT TGA T GTG CAC V GGC CCG G	TCA AGT S 660 TTT AAA F ACC TGG T	ACA TGT T 710 AAA TTT K	TTA AAT L AAA TTT K TTA AAT L GCT	ACA TGT T 67 GAA CTT E GAG CTC E	TAA I> 70 AAC TTG N> 720 GGG CCC G>
ACT TGA T ACT TGA T TGA T TCA	AAA TTT K 630 GTA CAT V ATT TAA I	AAC TTG N 680 ACA TGT T 7	ACT TGA T AGT TCA S GTA CAT V	GCA CGT A 64 AAA TTT K CAA GTT Q	CGA A 10 AAA TTT K 690 CAA GTT Q	ACC W ACT TGA T TAC ATG Y 740	AAT TTA N AAA TTT K GAC CTG D CTT	AGT S GAC CTG D TCA AGT S	CCG G GAA L DOO. AAT TTA N	ACT TGA T GTG CAC V GGC CCG G	TCA AGT S 660 TTT AAA F ACC TGG T	ACA TGT T 710 AAA TTT K	TTA AAT L AAA TTT K TTA AAT L GCT	ACA TGT T 67 GAA CTT E GAG CTC E	TAA I> 70 AAC TTG N> 720 GGG CCC G>

FIGURE 32 (2 of 5)

B-31 OSP A/ B-31 P-93

770			780			79	0		8	00			810		
•		•	•		•		•	•		•		•	•		•
GGT	CAC	CCC	ATG	GAT	GAA	AAG	CTT	ATT	AAA	AGT	AAA TTT	CTA	GAT	AAA	GCA
	GTG H			D								D	D	K	A>
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82	20		8	30			840			85	0		ε	360	
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		GAT													
		CTA												AGA S	TTT .
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	870			88	0		8	90		,	900			91	10
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		AGC													
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A	S	s	K	E	K	2	V	Α.	'n	E	L	L	_	1	V>
		920			930			94	40		9	50			960
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GGT	AAG	TCA	CAG	AAA	AGC	ATT	GGC	GAT	TTG	AAT.	TAA	GAT	GAA	AAT	CTT
		AGT			TCG S									TTA N	
G	K	S	Q	K	5	ם	G	D	<u>.</u>	14	14	D	Ŀ	14	L>
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ATG	ATG	CCA	GAA	GAT	CAA	AAA	TTA	CCT	GAG	GTT	• AAA	AAA	• TTA	GAT	AGC TOO
TAC	TAC	CCA GGT	GAA CTT	CTA	CAA GTT	AAA TTT	AAT	GGA	GAG CTC	CAA	TTT	AAA TTT	TTA	CTA	TCG
ATG TAC M	TAC	CCA GGT	GAA CTT	GAT CTA D	CAA GTT	AAA TTT	AAT	GGA	GAG CTC	CAA	TTT	AAA TTT	TTA	GAT CTA D	AGC TCG S>
TAC	TAC M	CCA GGT P	GAA CTT	CTA D	CAA GTT	AAA TTT	AAT L	GGA	GAG CTC E	CAA	TTT	AAA TTT K	TTA	CTA	TCG
TAC M 1010	TAC M	CCA GGT P	GAA CTT E	CTA D	CAA GTT Q	AAA TTT K	AAT L 30	GGA P	GAG CTC E	CAA V 040	TTT	AAA TTT K	TTA AAT L	CTA D	TCG S>
TAC M 1010 *	TAC M	CCA GGT P	GAA CTT E 1020	CTA D	CAA GTT Q	AAA TTT K 10	AAT L 30 TCT	GGA P GAG	GAG CTC E	CAA V 040 GAG	TTT K	AAA TTT K	TTA AAT L 1050	CTA D AAG	TCG S>
TAC M 1010 AAA TTT	TAC M AAA TTT	CCA GGT P	GAA CTT E 1020 TTT AAA	CTA D AAA TTT	CAA GTT Q CCT GGA	AAA TTT K 10 GTT CAA	AAT L 30 TCT AGA	GGA P GAG CTC	GAG CTC E 1 GTT CAA	CAA V 040 GAG CTC	TTT K AAA TTT	AAA TTT K TTA AAT	TTA AAT L 1050 GAT CTA	D AAG	TCG S> ATT TAA
TAC M 1010 *	TAC M	CCA GGT P	GAA CTT E 1020	CTA D AAA TTT	CAA GTT Q CCT GGA	AAA TTT K 10 GTT CAA	AAT L 30 TCT AGA	GGA P GAG CTC	GAG CTC E 1 GTT CAA	CAA V 040 GAG	TTT K AAA TTT	AAA TTT K TTA AAT	TTA AAT L 1050	D AAG	TCG S> ATT TAA
TAC M 1010 AAA TTT K	TAC M AAA TTT	CCA GGT P	GAA CTT E 1020 TTT AAA F	CTA D AAA TTT	CAA GTT Q CCT GGA	AAA TTT K 10 GTT CAA V	AAT L 30 TCT AGA	GGA P GAG CTC E	GAG CTC E 1 GTT CAA V	CAA V 040 GAG CTC	TTT K AAA TTT K	AAA TTT K TTA AAT	TTA AAT L 1050 GAT CTA D	D AAG	TCG S> ATT TAA
TAC M  1010 AAA TTT K	TAC M AAA TTT K	CCA GGT P GAA CTT	GAA CTT E 1020 TTT AAA F	CTA D AAA TTT K	CAA GTT Q • CCT GGA P	AAA TTT K 10 GTT CAA V	AAT L 30 TCT AGA S	GGA P GAG CTC E	GAG CTC E 1 GTT CAA V	CAA V 040 GAG CTC E	AAA TTT K	AAA TTT K TTA AAT L	TTA AAT L 1050 GAT CTA D	D AAG TTC K	TCG S> ATT TAA I>
TAC M  1010 AAA TTT K  10	TAC M AAA TTT K 60	CCA GGT P GAA CTT E	GAA CTT E 1020 TTT AAA F	CTA D AAA TTT K	CAA GTT Q CCT GGA P	AAA TTT K 10 GTT CAA V	AAT L 30 TCT AGA S 1080	GGA P GAG CTC E	GAG CTC E 1 GTT CAA V	CAA V 040 GAG CTC E 10	AAA TTT K  90 CCG	AAA TTT K TTA AAT L	TTA AAT L 1050 GAT CTA D 1 GAT	AAG TTC K 100	TCG S> ATT TAA I>
TAC M  1010 AAA TTT K  10 TTC AAG	AAA TTT K	CCA GGT P GAA CTT E	GAA CTT E 1020 TTT AAA F 1	AAA TTT K	CAA GTT Q CCT GGA P	AAA TTT K 10 GTT CAA V	AAT L 30 TCT AGA S 1080 GGA CCT	GGA P GAG CTC E	GAG CTC E  1  GTT CAA V  TTA	CAA V 040 GAG CTC E 10	AAA TTT K  CCG GGC	AAA TTT K TTA AAT L TTA AAT	TTA AAT L 1050 GAT CTA D GAT CTA	AAG TTC K	TCG S> ATT TAA I> TCT AGA
TAC M  1010 AAA TTT K  10 TTC AAG	TAC M AAA TTT K 60	CCA GGT P GAA CTT E	GAA CTT E 1020 TTT AAA F	AAA TTT K	CAA GTT Q CCT GGA P	AAA TTT K 10 GTT CAA V	AAT L 30 TCT AGA S 1080 GGA CCT	GGA P GAG CTC E	GAG CTC E  1  GTT CAA V  TTA	CAA V 040 GAG CTC E 10	AAA TTT K  CCG GGC	AAA TTT K TTA AAT L TTA AAT	TTA AAT L 1050 GAT CTA D GAT CTA	AAG TTC K	TCG S> ATT TAA I> TCT AGA
TAC M  1010 AAA TTT K  10 TTC AAG	AAA TTT K	CCA GGT P GAA CTT E	GAA CTT E 1020 TTT AAA F 1	AAA TTT K 070 AAC TTG	CAA GTT Q CCT GGA P	AAA TTT K 10 GTT CAA V	AAT L 30 TCT AGA S 1080 GGA CCT	GGA GAG CTC E GAA CTT E	GAG CTC E  1  GTT CAA V  TTA	CAA V 040 GAG CTC E 10	AAA TTT K  CCG GGC	AAA TTT K TTA AAT L TTA AAT	TTA AAT L 1050 GAT CTA D GAT CTA	AAG TTC K 100 AAA TTT	TCG S> ATT TAA I> TCT AGA
TAC M  1010 AAA TTT K  10 TTC AAG F	TAC M AAA TTT K 60 AAG TTC K	CCA GGT P GAA CTT E	GAA CTT E 1020 TTT AAA F 1 AAT N	AAA TTT K 070 AAC TTG N	CAA GTT Q CCT GGA P AAT TTA N	AAA TTT K 10 GTT CAA V	AAT L 30 * TCT AGA S 1080 * GGA CCT G	GAA GAA CTT E	GAG CTC E 1 GTT CAA V	CAA V 040 GAG CTC E 10 TCA AGT S	AAA TTT K 90 CCG GGC P	AAA TTT K TTA AAT L TTA AAT	TTA AAT L 1050 GAT CTA D GAT CTA D	AAG TTC K 100 AAA TTT K	TCG S> ATT TAA I> TCT AGA S> 50
TAC M  1010 AAA TIT K  10 TTC AAG F	TAC M  AAA TIT K  60 AAG TTC K	CCA GGT P GAA CTT E TCT	GAA CTT E 1020 TTT AAA F 1 AAT N	AAA TIT K 070 AAC TTG N 11	CAA GTT Q CCT GGA P AAT TTA N	AAA TTT K 10 GTT CAA V GTT CAA V TCA	AAT L 30 TCT AGA S 1080 CCT G	GGA P GAG CTC E GAA CTT E 130	GAG CTC E 1 GTT CAA V	CAA V 040 GAG CTC E 10 TCA AGT S	AAA TTT K  90 CCG GGC P 1140	AAA TTT K TTA AAT L TTA AAT L	TTA AAT L 1050 GAT CTA D GAT CTA D	AAG TTC K 100 AAA TTT K 11	TCG S> ATT TAA I> TCT AGA S> 50 • GTT
TAC M  1010 AAA TIT K  10 TTC AAG F	TAC M  AAA TIT K  60 AAG TIC K	CCA GGT P GAA CTT E TCT	GAA CTT E 1020 TTT AAA F 1 AAT N	AAA TTT K 070 AAC TTG N 11	CAA GTT Q CCT GGA P AAT TTA N	AAA TTT K 10 GTT CAA V GTT CAA V	AAT L 30 TCT AGA S 1080 GGA CCT G	GGA CTC E GAAA CTT E 130	GAGCTC E 1 GTT CAA V TTA AAT L	CAA V 040 GAG CTC E 10 TCA AGT S GACE TGT	AAA TTT K  90 CCG GGC P 1140	AAA TTT K TTA AAT L TTA AAT L	TTA AAT L 1050 GAT CTA D GAT CTA D	AAG TTC K 100 AAA TTT K 11	TCG S> ATT TAA I> TCT AGA S> 50 • GTT CAA

B-31 OSP / B-31 P-93

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	GTC	GCC R	ATA	CCT G	TAA I	ATA	CTT	GCA R	CTT	TTT	CTA	AAC L	CAA	CAA V	TAA	K>
	GTC Q	GCC R	ATA Y	CCT G	TAA I	ATA Y 1410	E	GCA R	E 14	TTT K 20	CTA D	AAC L 1	CAA V 430	CAA V	TAA I	K>
	GTC Q	GCC R	ATA Y 400	CCT G	TAA I •	ATA Y 1410 GCT	CTT E AAG	GCA R	E 14	TTT K 20	CTA D	AAC L 1 GAT	CAA V 430	CAA	TAA I	K> 1440 AAT
	Q Q . ATG	GCC R	ATA Y 400 TCA	G GGA	TAA I	ATA Y 1410 GCT CGA	E AAG	GCA R CTT	E 14 CAG	TTT K 20 ATA TAT	CTA D • CTT	AAC L 1 GAT CTA	CAA V 430 AAA TTT	CAA V CTT GAA	TAA I GAA CTT	K> 1440 AAT TTA
	GTC Q	GCC R	ATA Y 400 TCA	G GGA	TAA I AAA TTT K	ATA Y 1410 • GCT CGA A	E AAG TTC	GCA R CTT GAA L	CTT E 14 CAG GTC	TTT K 20 ATA TAT	CTA D CTT GAA L	AAC L 1 GAT CTA	V 430 AAA TTT K	CAA V CTT GAA L	TAA I GAA CTT	K> 1440 AAT TTA
	Q Q . ATG	GCC R	ATA Y 400 TCA AGT	G GGA	TAA I AAA TTT K	ATA Y 1410 • GCT CGA A	E AAG	GCA R CTT GAA L	CTT E 14 CAG GTC	TTT K 20 ATA TAT	CTA D CTT GAA L	AAC L 1 GAT CTA	CAA V 430 AAA TTT	CAA V CTT GAA L	TAA I GAA CTT	K> 1440 AAT TTA
	Q Q ATG	GCC R 3 GA1 CT/ D	400 TCA AGT S	GGA	TAA I AAA TTT K	ATA Y 1410 GCT CGA A	AAG TTC K	GCA R CTT GAA L	CTT E 14 CAG	TTT K 20 ATA TAT I 1470	CTA D CTT GAA L	AAC L 1 GAT CTA D	CAA V 430 AAA TTT K	CAA V CTT GAA L	GAA CTT E	K> 144C AAT TTA N>
	GTC O ATG TAC M	GCC R J GA1 CT7 D	400 TCA AGT	GGA GGA GGA GGA GGA GGA GGA GGA GGA GGA	TAA I AAA TTT K	ATA Y 1410 GCT CGA A 1	AAG TTC K 460	GCA R CTT GAA L	CTT E 14 CAG GTC Q	TTT K 20 ATA TAT I 1470	CTA D CTT GAA L	AAC L 1 GAT CTA D	AAA	CAA V CTT GAA L 80	GAA CTT E	K> 144C AAT TTA N>
	GTC O ATG TAC M	GCC R J GAT CTI D	400 TCA AGT A GTO	GGA	TAA I AAA TTT K A TCA	ATA Y 1410 GCT CGA A 1 GAG	AAG TTC K 460 TCT AGA	GCA R CTT GAA L	CTT E 14 CAG GTC Q	TTT K 20 ATA TAT I 1470 GAGA CTC	CTA D CTT GAA L G. ATT	AAC L  GAT CTA D  AAT	AAA TTT K 14 AAA TTT	CAA V CTT GAA L 80	GAA CTT E	K> 144C AAT TTA N>
	GTC Q ATG TAC M	GCC R J GA1 CTI D	400 TCA AGT A GTO	GGA GGA GGA GGTA GGTA V	TAA I AAA TTT K A TCA T AGT	ATA Y 1410 CGA A 1 GAC CTC	AAG TTC K 460 TCT AGA	GCA R CTT GAA L AAT	CTT E 14 CAG GTC Q	TTT K  20 . ATA TAT I  1470 G GAG A CTO E	CTA D CTT GAA L CTAA I	AAC L 1 GAT CTA D	AAA TTT K 14 AAA TTT	CAA V CTT GAA L 80	GAA CTT E TCA AGT	K> 144C AAT TTA N> TCT AGA
	GTC O ATG TAC M	GCC R J GA1 CTI D	400 TCA AGT A GTO	GGA	TAA I AAA TTT K A TCA T AGT	ATA Y 1410 CGA A 1 GAC CTC	AAG TTC K 460 TCT AGA	GCA R CTT GAA L AAT	CTT E 14 CAG GTC Q	TTT K  20 . ATA TAT I  1470 G GAG A CTO E	CTA D CTT GAA L G. ATT	AAC L 1 GAT CTA D	AAA TTT K 14 AAA TTT	CAA V CTT GAA L 80	GAA CTT E TCA AGT	K> 144C AAT TTA N> TCT AGA
	GTC Q ATG TAC M TT/ AAT L	GCC R I GAT CTA D	ATA Y 400 TCA AGT AGT V	GGA GGA GGA GGA GGA V	TAA I AAA TTT K A TCA I AGI	ATA Y 1410 GCT CGA A 1 GAG CTC	AAG TTC K 460 TCT AGA TCT AGA	GCA R CTT GAA L TT7	CTT E 14 CAG GTC Q	TTT K  20  ATA TAT I  1470 A CTO E	CTA D CTT GAA L TAA I 1520	GAT CTA D AAT N	AAA TTT K 14 AAA TTT K	CTT GAA L 80 AAT N	GAA CTT E TCA AGT S	K> 144C AAT TTA N> TCT AGA S>
	GTC Q ATG TAC M TT/ AAT L	GCCC R  1  GAN CTM D  A AA I TT K	ATA Y 400 TCA AGT CA CTCA CTCA AGT CA CTCA CA CTCA CA CTCA CA C	GGA	TAA I AAA TTT K A TCA A TCA A TCCA A AGA	ATA Y 1410 GCT CGA A 1 GAG TCT E	AAG ATC K 460 TCT AGA S 15	GCA R CTT GAA L TTX N G10	CTT E 14 CAG GTC Q . TTT A AAA	TTT K  20  ATA TAT I  1470 A CTO E A GTA T CA	CTA D CTT GAA L TAA I 1520 A GCT	AAC L 1 GAT CTA D AAT N 1 GTTA	AAA TTT K 14 AAA TTT K 14 AAA TTT K	CAA V CTT GAA L 80 AAT N 1530	GAA CTT E TCA AGT S	K> 144C AAT TTA N> TCT AGA S> GAT CTA
	GTC Q ATG TAC M TT/ AAT L	GCCC R  1  GAN CTM D  A AA I TT K	ATA Y 400 TCA AGT CA CTCA CTCA AGT CA CTCA CA CTCA CA CTCA CA C	GGA	TAA I AAA TTT K A TCA A TCA A TCCA A AGA	ATA Y 1410 GCT CGA A 1 GAG TCT E	AAG ATC K 460 TCT AGA S 15	GCA R CTT GAA L TTX N G10	CTT E 14 CAG GTC Q . TTT A AAA	TTT K  20  ATA TAT I  1470 A CTO E A GTA T CA	CTA D CTT GAA L TAA I 1520 A GCT	AAC L 1 GAT CTA D AAT N 1 GTTA	AAA TTT K 14 AAA TTT K 14 AAA TTT K	CAA V CTT GAA L 80 AAT N 1530	GAA CTT E TCA AGT S	K> 144C AAT TTA N> TCT AGA S>

B-31 OSP A/ B-31 P-93

1560 1570 1540 1550 1580 AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA GAT TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT CTA S S N D W R L A K F S P K N L D> 1600 1610 1620 GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT TCT CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA AGA E F I L S E N K I M P F T S F S> 1660 1670 1650 1640 GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA GTT CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT CAA -V R K N F I Y L Q D E F K S L V> 1690 1700 1710 1720 ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG GGT CAC C TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC CCA GTG G I L D V N T L K K V K G H X>

B-31 OSP B/ B-31 P41 (122-234)

OSPB/Fla122-234

Sequence Range: 1 to 1180

20 . 30 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT . A Q K G A E S I G S Q K E N D L> 70 80 \_\_\_\_ 60 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 120 110 100 130 140 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 170 160 150 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 210 220 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 260 270 • GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 300 310 320 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA LTVSADLNTVTLEAFD> 350 360 370 380 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

#### B-31 OSP B/ B-31 P41 (122-234)

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	161	101	AGI	116	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GIT	TAT	TGT	CTA	CGA
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	D	S	T	s	T	L	T	1	s	A	D	S	K	K	T	K>
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	GAT	TTG	GTG	TTC	TTA	ACA	GAT	GGT	ACA	ው ውጥ	ארא	GTA	CAB.	•	•	
	CTA	AAC	CAC	AAG	AAT	TGT	CTA	CCA	TGT	TAA	TGT	CAT	CAA	CAA	TAC	AAC
	D	L	v	F	L	T	D	G	T	I	T	v	Q	Q	YIG	N>

FIGURE 33 (2 of 4)

### B-31 OSP B/ B-31 P41 (122-234)

770	780			7	90		1	800			810				
•		•	•		•		•	•		•		•	•		•
ACA	GCT	GGA	ACC	AGC	CTA	GAA	GGA	TCA	GCA	AGT	GAA	ATT	AAA	AAT	CTT
TGT T		CCT	TGĢ	TCG S		E									
•	A	G	•	3	ь	£	G	S	A	s	. E	I	K	N	L>
83	20	•	1	B30 •			840		•	8	50	•	1	360	
TCA	GAG	CTT	λλλ	AAC	GCT	TTA	AAA	GGT	CAC	ccc	ATG	GCT	CEL	тат	220
AGT	CTC	GAA	TTT	TTG	CGA	AAT	TTT	CCA	GTG	GGG	TAC	CGA	GTT	ATA	TTG
· s	E	L	K	N	A	L		G					Q	Y	N>
	870			88	30		1	390			900			91	0
•	•		•		•	•		•		•	•		•		•
CAA	ATG	CAC	ATG	TTA	TCA	AAC	AAA	TCT	GCT	TCT	CAA	AAT	GTA	AGA	ACA
		GTG												TCT	TGT
Q	M	н	M	L	S	N	K	S	A	s	Q	N	V	R	T>
	9	920			930			94	0		9	950			960
•		•		•	•		•		•	•		•		•	•
GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	AAA	ATT	AAC	ACA	CCA	GCA	TCA
		CTC													
A	E	E	L	G	М	Q	P	A	K	I	N	T	P	Α	S>
		97	70		9	980			990			100	00		
	•	_	•	•		•		•	•		•		•	•	
CTT	TCA	GGG	· CTT	CAA	GCG	· TCT	TGG	ACT	• TTA	AGA	GTT	CAT	GTT	• GGA	GCA
GAA	AGT	GGG	CTT GAA	GTT	GCG	• TCT AGA	ACC	TGA	TTA	TCT	CAA	CAT GTA	GTT CAA	CCT	CGT
CTT GAA L	TCA AGT S	GGG	· CTT	CAA GTT Q	GCG	· TCT	TGG ACC W	• ACT TGA T	• TTA	TCT	GTT CAA V	CAT	GTT	GGA CCT G	GCA CGT A>
GAA	AGT	GGG CCC G	CTT GAA	GTT	GCG	• TCT AGA	W W	TGA	TTA AAT L	TCT	CAA	CAT GTA H	GTT CAA	CCT	CGT
GAA L 1010	AGT S	GGG CCC G	CTT GAA L	GTT Q	GCG CGC A	TCT AGA S	ACC W	TGA T	TTA AAT L	TCT R	CAA V	CAT GTA H	GTT CAA V	CCT G	CGT A>
GAA L 1010	AGT S CAA	GGG CCC G	CTT GAA L 1020	GTT Q GCT	GCG CGC A	TCT AGA S	ACC W 30 • GTA	TGA T	TTA AAT L 10	TCT R 040 TAT	CAA V GCA	CAT GTA H	GTT CAA V 1050	CCT G	CGT A>
GAA L 1010	AGT S CAA	GGG CCC G	CTT GAA L 1020	GTT Q GCT	GCG CGC A	TCT AGA S 103	ACC W 30 GTA CAT	TGA T AAT TTA	TTA AAT L 10 ATT TAA	TCT R 040 TAT ATA	CAA V GCA CGT	CAT GTA H GCT CGA	GTT CAA V 1050 AAT TTA	CCT G GTT -CAA	A> GCA CGT
GAA L 1010 ACC TGG	AGT S CAA GTT	GGG CCC G	CTT GAA L 1020 GAA CTT	GTT Q GCT CGA	GCG CGC A	TCT AGA S	ACC W 30 • GTA	TGA T	TTA AAT L 10	TCT R 040 TAT	CAA V GCA	CAT GTA H	GTT CAA V 1050	CCT G	CGT A>
GAA L 1010 ACC TGG	AGT S CAA GTT Q	GGG CCC G	CTT GAA L 1020 GAA CTT E	GTT Q GCT CGA	GCG CGC A	TCT AGA S 103 GCT CGA A	ACC W 30 GTA CAT	TGA T AAT TTA	TTA AAT L 10 ATT TAA	TCT R 040 TAT ATA	CAA V GCA CGT A	CAT GTA H GCT CGA	GTT CAA V 1050 AAT TTA N	CCT G GTT -CAA	A> GCA CGT
GAA L 1010 ACC TGG T	AGT S CAA GTT Q	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E	GTT Q GCT CGA A	GCG CGC A ATT TAA I	TCT AGA S 103 GCT CGA A	ACC W 30 GTA CAT V	TGA T AAT TTA N	TTA AAT L 10 ATT TAA I	TCT R 040 TAT ATA Y	CAA V GCA CGT A	CAT GTA H GCT CGA A	GTT CAA V 1050 AAT TTA N	GTT -CAA V	CGT A> GCA CGT A>
GAA L 1010 ACC TGG T 100	AGT S CAA GTT Q CTT	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10	GTT Q GCT CGA A 070	GCG CGC A ATT TAA I	TCT AGA S 103 GCT CGA A GGA	ACC W 30 GTA CAT V LOB0	TGA T AAT TTA N	TTA AAT L 10 ATT TAA I ACT	TCT R 040 TAT ATA Y 109	CAA V GCA CGT A	CAT GTA H GCT CGA A	GTT CAA V L050 AAT TTA N	GTT CAA V	CGT A> GCA CGT A>
GAA L 1010 ACC TGG T 100	AGT S CAA GTT Q CTT	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10	GTT Q GCT CGA A O70 GGT CCA	GCG CGC A ATT TAA I	TCT AGA S 103 GCT CGA A GGA CCT	GTA CAT V	TGA T AAT TTA N CAA GTT	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109	GCA GCA CGT A CAG GTC	CAT GTA H GCT CGA A	GTT CAA V L050 AAT TTA N	GTT CAA V	CGT A> GCA CGT A>
GAA L 1010 ACC TGG T 100 AAT TTA N	CAA GTT Q CTT GAA L	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10	GTT Q GCT CGA A O70 GGT CCA G	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A GGA CCT	GTA CAT V LOBO GCT CGA A	TGA T AAT TTA N CAA GTT Q	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109 GCT CGA A	CAA V GCA CGT A CAG GTC	CAT GTA H GCT CGA A GCT CGA	GTT CAA V LOSO AAT TTA N 13	GTT CAA V	GCA CGT A> GTT CAA V>
GAA L 1010 ACC TGG T 100 AAT TTA N	CAA GTT Q CTT GAA	GGG CCC G GAT CTA D	CTT GAA L 1020 GAA CTT E 10	GTT Q GCT CGA A O70 GGT CCA	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A GGA CCT	GTA CAT V LOBO GCT CGA A	TGA T AAT TTA N CAA GTT	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109 GCT CGA A	GCA GCA CGT A CAG GTC	CAT GTA H GCT CGA A GCT CGA	GTT CAA V LOSO AAT TTA N 13	GTT CAA V	GCA CGT A> GTT CAA V>
GAA L 1010 ACC TGG T 100 AAT TTA N	CAA GTT Q CTT GAA L	GGG CCC G GAT CTA D TTC AAG F	CTT GAA L 1020 GAA CTT E 10 TCT AGA S	GCT CGA A O70 GGT CCA G	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A CCT G GAA	GTA CAT V LOBO GCT CGA A 1:	TGA T AAT TTA N CAA GTT Q 130 GCT	TTA AAT L 10 ATT TAA I ACT TGA T CAA	TAT ATA Y 109 GCT CGA A	GCA CGT A CAG GTC Q	CAT GTA H GCT CGA A GCT CGA A	GTT CAA V 1050 AAT TTA N 13 GCA CGT A	GTT CAA V 100 CCG GGC P 115	GCA CGT A> GTT CAA V> 60 .
GAA L 1010 ACC TGG T 100 AAT TTA N	CAA GTT Q CTT GAA L	GGG CCC G GAT CTA D TTC AAG F	CTT GAA L 1020 GAA CTT E 10 TCT AGA S	GCT CGA A O70 GGT CCA G	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 103 GCT CGA A CCT G GAA	GTA CAT V LOBO GCT CGA A 1:	TGA T AAT TTA N CAA GTT Q 130 GCT	TTA AAT L 10 ATT TAA I ACT TGA T CAA	TAT ATA Y 109 GCT CGA A	GCA CGT A CAG GTC Q	CAT GTA H GCT CGA A GCT CGA A	GTT CAA V 1050 AAT TTA N 13 GCA CGT A	GTT CAA V 100 CCG GGC P 115	GCA CGT A> GTT CAA V> 60 .

B-31 OSP B/ B-31 P41 (122-234)

GCA CCT TCT CAA GGC GGA GTT GGT CAC C
CGT GGA AGA GTT CCG CCT CAA CCA GTG G
A P S Q G G V G H X>

FIGURE 33 (4 of 4)

76/33 B-31 OSP B / B-31 P41 (122-295)

Sequence Range: 1 to 1363

20 30 10 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> 60 60 70 80 90 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA-AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 100 110 120 130 • CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 170 180 150 160 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 260 270 280 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 300 • 310 320 300 290 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 360 . 370 350 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

### B-31 OSP B / B-31 P41 (122-295)

		390	)		4	00			410			420	)			130
	•	•		•		•	•				•			•		_
	ATA	ACA	GAG	GAA	ACT	CIC	AAA	GCT	' AAT	, YYY	TŢ	GAC	TC	AAC	. AAA	TTA
	IVI	101	CIC	. CII	IGA	GAG	1-1-1	CGA	TTA	TTT	' AAT	CTO	AG7	TTC	TIT	` AAT
	I	T	Ε	E	T	L	K	A	N	K	L	D	S	K	K	
			440			450			4	60			470			480
r.	•		•		•	•		•		•	•				•	
•	ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTI	GAA	TAC	TCA	CAA	ATA	ACA	GAT	GCT
	101	101	VQ1	116	CCJ	IGA	161	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
	T <sub>.</sub>	R	S	N	G	· T	T	L	E	Y	S	Q	I	T	D	
			4	90		!	500			510			5	20		
		*		•	•		•		•	•		•			•	
	GAC	AAT	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	ÅAG	CTT
	CIG	IIA	CGA	101	1.1.1	CGT	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
	D	N	A	T	К	Α	V	E	T	L	K	N	S	I	ĸ	L>
	530			540	٠		5	50		9	560			570	•	
	•		•	•		•		•	•		•		•			•
	GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
	CII	CCI	ICA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TTT	CTT	CCA
	E	G	S	L	V	V	G	K	T	T	v	E	I	K	E	G>
	5	80		:	590			600			6:	10			520	•
		•	•		•		*	•		•		•	•		•	
	ACT	GTT	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	AAA	GTC
	TGA T	CAA	IGA	GAI	111	TCT	CTT	TAA	CTT	TTT	CTA	CCT	TTT	CAT	TTT	CAG
	1	V	T	L	ĸ	R	E	I	E	K	D	G	K	v	K	V>
		630			64	0		(	550			660			67	'n
	•	•		•		•	•		•		•	•		•		_
	TTT	TTG	AAT	GAC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA
	777	WYC	IIA	CIG	TGA	CGT	CCA	AGA	TTG	TTT	TTT	TGT	CCA	TTT	ACC	CTT
	F	. 1	N	D	T	A	G	S	N	K	K		G	K	W	E>
		6	80			690			70	0		7	10			720
	•		*		•	•		•		•	•		•		•	
	GAC	AGT	ACT	AGC	ACT	TTA	ACA	ATT	AGT	GCT	GAC	AGC	AAA	AAA	ACT	AAA
	CIG	ICA	IGA	ICG	TGA	AAT.	TGT	TAA	TCA	CGA	CTG	TCG	TTT	TTT	TGA	TTT
	D	S	T	S	T	L	T	I	S	A	D	S	ĸ	K	T	K>
			73	0		7	40			750	ı		76	· n		
		•	_	•	•		•		•	•		•		•		
	GAT	TTG	GTG	TTC	TTA .	ACA	GAT	GGT	ACA	ATT	ACA	GTA	CAA	CAA	TAC	226
	CIA	MAC	CAC	AAG	AAT	TGT	CTA	CCA	TGT	TAA	TGT	CAT	GTT	GTT	ATG	ተጥር
	D	L	v	F	L	T	D	G	T	т	T	37		~~		

FIGURE 34 (2 of 4)

78//33

B-31 OSP B / B-31 P41 (122-295)

770		_	780			79	0		ε	300			810		•
					GAT	CTT	CCT	AGT	CGT	AGT TCA S	CTT				
82	20	•	8	30		•	840		•	85	0	•	8	860	
				TTG	CGA	TAA	TTT	CCA	GTG	CCC GGG P	TAC	CGA	GTT	ATA	TTG
•	870		•	88	30	•	8	390		•	900		•	91	10
							TTT		CGA	TCT AGA S	GTT				TGT
	9	20		_	930			94	10	_	9	50			960
	CTT			CCT		GTC	GGA	CGT	TTT	TTA AAT I		TGT			
	_	91	70		9	80			990		_	100	00	_	
		GGG	CTT GAA	GTT	GCG	TCT AGA	ACC	TGA	TTA AAT	AGA TCT R		CAT GTA	• GTT		
GAA	AGT	GGG CCC G	CTT GAA	GTT	GCG CGC	TCT AGA	W W	TGA	TTA AAT L	TCT	CAA	CAT GTA H	GTT CAA	CCT	CGT
GAA L 1010 ACC	AGT S CAA	GGG CCC G	CTT GAA L 1020 GAA	GTT Q GCT	GCG CGC A	TCT AGA S 103	ACC W 30 GTA CAT	TGA T AAT TTA	TTA AAT L 10	TCT R 040 TAT ATA	CAA V GCA	CAT GTA H	GTT CAA V LOSO	GTT	CGT A>  GCA CGT
GAA L 1010 ACC TGG	AGT S CAA GTT Q	GGG CCC G	CTT GAA L 1020 GAA CTT E	GTT Q GCT CGA	GCG CGC A	TCT AGA S 103 GCT CGA A	ACC W 30 GTA CAT	TGA T AAT TTA	TTA AAT L 10 ATT TAA	TCT R 040 TAT ATA	CAA V GCA CGT A	CAT GTA H GCT CGA	GTT CAA V LOSO AAT TTA N	CCT G GTT CAA	CGT A>  GCA CGT
GAA L 1010 ACC TGG T 100	AGT S CAA GTT Q CTT	GGG CCC G GAT CTA D	GAA CTT E	GTT Q GCT CGA A	GCG CGC A ATT TAA I	TCT AGA S 10: GCT CGA A GGA CCT	GTA CAT V	TGA T AAT TTA N CAA GTT	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y	GCA CGT A CAG CAG GTC	CAT GTA H GCT CGA A	GTT CAA V LOSO AAT TTA N	GTT CAA V	CGT A> GCA CGT A> GTT CAA
GAA L 1010 ACC TGG T 100 AAT TTA N	CAA GTT Q CTT GAA	GGG CCC G GAT CTA D TTC AAG F	GAA CTT E	GTT Q GCT CGA A D70 GGT CCA	GCG CGC A ATT TAA I GAG CTC E	TCT AGA S 10: GCT CGA A GGA CCT	GTA CAT V 1080 GCT CGA A	TGA T AAT TTA N CAA GTT	TTA AAT L 10 ATT TAA I ACT TGA	TCT R 040 TAT ATA Y 109 GCT CGA A	GCA CGT A CAG CAG GTC	CAT GTA H GCT CGA A GCT CGA	GTT CAA V LOSO AAT TTA N 1: GCA CGT	GTT CAA V	CGT A> GCA CGT A> GTT CAA V>

FIGURE: 34 (3 of 4)

#### B-31 OSP B / B-31 P41 (122-295)

..... 1180 1170 1190 1160 GCA CCT TCT CAA GGC GGA GTT AAT TCT CCT GTT AAT GTT ACA ACT ACA CGT GGA AGA GTT CCG CCT CAA TTA AGA GGA CAA TTA CAA TGT TGA TGT A P S Q G G V N S P V N V T T T> 1210 1220 1230 • • • GTT GAT GCT AAT ACA TCA CTT GCT AAA ATT GAA AAT GCT ATT AGA ATG CAA CTA CGA TTA TGT AGT GAA CGA TTT TAA CTT TTA CGA TAA TCT TAC V D A N T S L A K I E E N A I R M> 250 1260 1270 1280 1250 1299 ATA AGT GAT CAA AGG GCA AAT TTA GGT GCT TTC CAA AAT AGA CTT GAA TAT TCA CTA GTT TCC CGT TTA AAT CCA CGA AAG GTT TTA TCT GAA CTT I S D Q R A N L G A F Q N R L E> 1310 1320 1300 1330 TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA AAA GCA TCT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT TTT CGT AGA S I K N S T E Y A I E N L K A S> 1350 1360 TAT GCT CAA ATA GGT CAC C ATA CGA GTT TAT CCA GTG G Y A Q I G H X>

PCT/US94/12352

80/133

B-31 OSP B/ B-31 P41 (140-234)

Sequence Range: 1 to 1141

20 30 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> 60 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CIT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 120 110 100 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAA AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAR TTA CCA TTA TTT LPAVTEDSVSLFNGNK> 170 160 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 260 250 270 280 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AA2 CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 310 320 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA LTVSADLNTVTLEAFD 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

PCT/US94/12352

81/133

B-31 OSP B/ B-31 P41 (140-234)

400 410 420 390 ATA ACA GAG GAA ACT CTC AAA GCT AAT AAA TTA GAC TCA AAG AAA TTA TAT TGT CTC CTT TGA GAG TTT CGA TTA TTT AAT CTG AGT TTC TTT AAT I T E E T L K A N K L D S K K L> 460 470 450 440 • ACA AGA TCA AAC GGA ACT ACA CTT GAA TAC TCA CAA ATA ACA GAT GCT TGT TCT AGT TTG CCT TGA TGT GAA CTT ATG AGT GTT TAT TGT CTA CGA TRSNGTTLEYS\_QITDA> 500 . 510 490 GAC AAT GCT ACA AAA GCA GTA GAA ACT CTA AAA AAT AGC ATT AAG CTT CTG TTA CGA TGT TTT CGT CAT CTT TGA GAT TTT TTA TCG TAA TTC GAA D N A T K A V E T L K N S I K L> 540 550 560 GAA GGA AGT CTT GTA GTC GGA AAA ACA ACA GTG GAA ATT AAA GAA GGT CTT CCT TCA GAA CAT CAG CCT TTT TGT TGT CAC CTT TAA TTT CTT CCA EGSLVVGKTTVEIKEG> 610 620 580 590 600 ACT GTT ACT CTA AAA AGA GAA ATT GAA AAA GAT GGA AAA GTA AAA GTC TGA CAA TGA GAT TTT TCT CTT TAA CTT TTT CTA CCT TTT CAT TTT CAG T V T L K R E I E K D G K V K V> 660 640 650 TTT TTG AAT GAC ACT GCA GGT TCT AAC AAA AAA ACA GGT AAA TGG GAA AAA AAC TTA CTG TGA CGT CCA AGA TTG TTT TTT TGT CCA TTT ACC CTT F L N D T A G S N K K T G K W E> 700 680 690 700 710 GAC AGT ACT AGC ACT TTA ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA CTG TCA TGA TCG TGA AAT TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT D S T S T L T I S A D S K K T K> 730 740 750 GAT TTG GTG TTC TTA ACA GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC CTA AAC CAC AAG AAT TGT CTA CCA TGT TAA TGT CAT GTT ATG TTG D L V F L T D G T I T V Q Q Y N>

FIGURE 35 (2 of 3)

#### B-31 OSP B/ B-31 P41 (140-234)

770		780 • • • • • • • • • • • • • • • • • • •			•	79	0		8	00			810		•
				AGC TCG											
<b>T</b>	A	G	T	S	L	E	G	S	A	S	E	I	K	N	L>
82	20	•	8	30		•	840		•	85	0	•	8	860	
				AAC TTG											
S				N								A	S		N>
•	870			88	30	•	8	390		•	900		•	91	10
				GAA											
CAT				CTT											
V	R	T	A	E	E	L	G	M	Q	P	A	K	I	N	T>
•	;	T A E		•	930		•	94	10		9	50		•	960
				TCA											
GGT	CGT			AGT											
P	A	S	L	s	G	L	Q	Α.	S	W	T	L	R	V	H>
		9.	70		9	980			990			100	00		
	•		•	•		. •		•	•		•		•	•	
				CAA GTT											
V	G	A	TGG	Q		E			A				Y	A	
•	J	••	•	~		_		_	•••	•	•	_	-	••	
1010		:	1020			10	30		10	040		_ :	1050		
እአጥ	CTT	# CCA	* አአጥ	ርጥጥ	TTC	TCT	GGT	GAG	GG A	ecm c	CAA	ACT	GCT	CAG	GCT
				GAA											
				L									A		
10										10	20				
	60	_	1	070		_	1080		••	10	-	_	1	100	
GC A	•	• GTT	_	•	CCT	•	•				•	•		•	GCA
	• CCG		CAA	GAG		GTT	CAA	CAG	GAA	GGA	• GCT		CAG	• CCA	
CGT	ccg GGC	CAA	CAA	GAG	CCA	GTT CAA	CAA GTT	CAG GTC	GAA CTT	GGA CCT	• GCT CGA	GTT	CAG GTC	CCA GGT	CGT
CGT A	CCG GGC P	CAA V	CAA GTT Q	GAG CTC E	CCA G	GTT CAA V	CAA GTT Q	CAG GTC Q	GAA CTT E	GGA CCT G	GCT CGA A	GTT	CAG GTC	CCA GGT	CGT
CGT A	CCG GGC P	CAA V	CAA GTT Q	GAG CTC E	CCA G 20	GTT CAA V	CAA GTT Q	CAG GTC Q 130	GAA CTT E	GGA CCT G	GCT CGA A	GTT Q	CAG GTC	CCA GGT	CGT
CGT A	CCG GGC P	CAA V ACA	CAA GTT Q	GAG CTC E 11:	CCA G 20 TCT	GTT CAA V	CAA GTT Q	CAG GTC Q 130	GAA CTT E	GGA CCT G	GCT CGA A 1140	GTT Q C	CAG GTC	CCA GGT	CGT
CGT A • CCT GGA	CCG GGC P 1110 GCT CGA	CAA V ACA TGT	CAA GTT Q GCA CGT	GAG CTC E	CCA G 20 TCT AGA	GTT CAA V	CAA GTT Q 1	CAG GTC Q 130	GAA CTT E	GGA CCT G	GCT CGA A 1140 CAC GTG	GTT Q C G	CAG GTC	CCA GGT	CGT

FIGURE 35 (3 of 3)

PCT/US94/12352

83/133

B-31 OSP B/ B-31 P41 (140 -295)

Sequence Range: 1 to 1324

10 20 30 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT AQKGAESIGSQKENDL> 60 80 70 70 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 110 120 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 160 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 210 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA ATIDQVELKGTSDKN N> 260 250 270 280 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 290 320 300 310 330 • TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA LTVSADLNTVTLEAFD> 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT ASNQKISSKVTKKQGS>

FIGURE 36 (1 of 4)

#### B-31 OSP B/ B-31 P41 (140 -295)

		390			4	00			410			420			4	20
	• .	ACA GAG		•	_	•	*		•		•	•		•	*	30
	ATA	ACA	GAG	GAA	ACT	CTC	AAA	GCT	AAT	AAA	TTA	GAC	TCA	AAG	AAA	TTA
	TAT	TGT	CTC	CTT	TGA	GAG	TTT	CGA	TTA	TTT	AAT	CTG	AGT	TTC	TTT	AAT
	I	T	E	E	T	L					L		S	K	ĸ	
			440			450			4	60			470			480
4	. •		•		•	•		•		•	•		•		•	
•	ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA	TAC	TCA	CAA	ATA	ACA	GAT	GCT
	TGT	TCT	AGT	TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
	T	R	S	N	G	T	T	L	E	¥	· s-	Q -	I	T	D	A>
			49	90		9	500			510			5:	20		•
		•		•	•		•		•	•		•		•	•	
	GAC	TAA	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	CTT
	CTG	TTA	CGA	TGT	TTT								TCG	TAA	TTC	GAA
	D	N	A	T	K	Α	V	E	T	L	K	N	s	I	K	L>
	530			540			5	50		9	560			570		
	•		•	•		•		•	•		•		•	•		•
	GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
	CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT					TAA	TTT	CTT	CCA
	E	G	S	L	V	V	G	K	T	T	V	E	I	K	E	G>
	58	80		5	590			600			61	0		6	520	
		•	•		•		•	•		•		•	•		•	
	TCA	CAA	AC1	CIA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	AAA	GTC
	T	V	T	L	TTT	R	CTT	TAA	CTT							
	•	•	•		K	Α.	<b>E</b> .	1	L	K	D	G.	K	V	K	۷>
		630			64	0		6	550			660			67	70
	*			•		•	•		*		•	•		•		•
	111	AAC	AAT.	CTC	ACT	GCA	GGT	TCT	AAC	AAA	AAA	ACA	GGT	AAA	TGG	GAA
	F	L	N	D	TGA T	A		AGA S	n N	K	K					
	•	_	••	-	•	Λ	G	3	14	ν.		T	G	K	W	E>
		. 6	80			690			70	0		7	10			720
	~		•		•			•		•	•		•		•	•
	CTC	TCA	ACT.	AGC	ACT	TTA	ACA	ATT	AGT	GCT	GAC	AGC	AAA	AAA	ACT	AAA
	D	S	T	S	TGA T	L	T		TCA							
			•	3	•	U	•	1	5	A	D	S	K	K	T	K>
		_	73	0	_	7	40			750			76	0		
	C1 T	- -	C.T.C	*	*		•		•	•		•		•	•	
	CT3	716	CVC	ANC	ATT	ACA	GAT	GGT	ACA	TTA	ACA	GTA	CAA	CAA	TAC	AAC
	D	L	V	F	AAT L	T	D	CCA G	TGT	TAA						
		_	•	•	u	-	ע	9	1	1	T	v	Q	Q	Y	N>

FIGURE 36 (2 of 4)

#### B-31 OSP B/ B-31 P41 (140 -295)

770			780			79	90		8	300			810		
•		• • • r GGA ACC AGC			•		•	•		•		•	•		•
ACA	GCT	GGA	ACC	AGC	CTA	GAA	GGA	TCA	GCA	AGT	GAA	ATT	AAA	AAT	CTT
TGT	CGA	CCT	TGG	TCG	GAT	CTT	CCT	AGT	CGT	TCA	CTT	AAT	TTT	TTA	GAA
T	A	G	T	s	L	E	G	S	A	S	E	I.	K	N	L>
82	20		ε	30			840			85	50		8	360	
	•	•		•		•	•		•		•	•		•	
TCA	GAG	CTT	AAA	AAC	GCT	TTA	AAA	GGT	CAC	CCC	ATG	GCT	TCT	CAA	AAT
AGT	CTC	GAA	TTT	TTG	CGA.	AAT	TTT	CCA	GTG	GGG	TAC	CGA	AGA	GTT	TTA
s	E	L	K	N	Α	L	K	G	H,	p"	H	A	S	Q	N>
	870			88	30 -		8	390			900			93	0
•	•	• • • GA ACA GCT GAA CT TGT CGA CTT			*	•		*		•	•		•		•
CAT	TCT	TGT	CGA	CTT	CTC	GAA	CCT	TAC	GTC	GGA	CGT	TTT	TAA	TŢG	TGT
V	R	T	A	E	E	L	G	М	Q	P	λ	K	I	N	T>
	9	320			930			94	0		9	50			960
•		•		•	•		•		•	*		•		•	•
					GGG										
	CGT	AGT			CCC										
P	Α	S	L	S	G	L	Q	A	S	W	T	L	R	V	H>
		91	70		9	80			990			100	00		
•	•		•	•		*		•	•		•		•	•	
					GAT										
		•			CTA										
V	G	A	T	0	n	Ε	Α	T	- 7	37	N				A>
1010				_		_	••	•	^	•	41	I	Y	A	
		;	1020	_	-	10:				040		_	Y 1050	A	
•		•	•	-	•	10:	30	•	. 10	040		•	1050	•	•
		• GCA	AAT	CTT	TTC	10: TCT	30 • GGT	• GAG	. 10	GCT	CAA	ACT	LOSO • GCT	CAG	GCT
	CAA	• GCA	AAT	CTT	• TTC AAG	10: TCT AGA	30 • GGT CCA	GAG CTC	GGA CCT	GCT CGA	CAA GTT	ACT	LOSO • GCT	CAG	GCT
		• GCA	AAT	CTT	• TTC AAG	10: TCT AGA	30 • GGT CCA	GAG CTC	. 10	GCT CGA	CAA GTT	ACT	LOSO • GCT	CAG GTC	GCT
TTA	CAA V	• GCA CGT	AAT TTA N	CTT GAA	• TTC AAG	TCT AGA S	30 • GGT CCA	GAG CTC E	GGA CCT G	GCT CGA	CAA GTT Q	ACT TGA	GCT CGA A	CAG GTC	• GCT CGA
TTA N 10	CAA V 60	GCA CGT A	AAT TTA N	CTT GAA L	TTC AAG F	10: TCT AGA S	GGT CCA G	GAG CTC E	GGA CCT G	GCT CGA A	CAA GTT Q	ACT TGA T	GCT CGA A	CAG GTC Q	GCT CGA A>
TTA N 100 GCA	CAA V 60 • CCG	GCA CGT A	AAT TTA N	CTT GAA L	TTC AAG F	10: TCT AGA S	GGT CCA G	GAG CTC E	GGA CCT G	GCT CGA A 109	CAA GTT Q	ACT TGA T	GCT CGA A	CAG GTC Q	GCT CGA A>
TTA N 100 GCA CGT	CAA V 60 • CCG GGC	GCA CGT A GTT CAA	AAT TTA N 10 CAA GTT	CTT GAA L 070 GAG CTC	TTC AAG F	10: TCT AGA S	GGT CCA G 1080 CAA GTT	GAG CTC E	GGA CCT G GAA CTT	GCT CGA A 109 GGA CCT	CAA GTT Q 90 • GCT CGA	ACT TGA T	GCT CGA A 11 CAG GTC	CAG GTC Q 100 • CCA GGT	GCT CGA A> GCA CGT
TTA N 100 GCA CGT	CAA V 60 • CCG	GCA CGT A GTT CAA	AAT TTA N 10 CAA GTT	CTT GAA L	TTC AAG F	10: TCT AGA S	GGT CCA G 1080 CAA GTT	GAG CTC E	GGA CCT G	GCT CGA A 109 GGA CCT	CAA GTT Q 90 • GCT CGA	ACT TGA T	GCT CGA A	CAG GTC Q 100 • CCA GGT	GCT CGA A>
TTA N 100 GCA CGT A	CAA V 60 • CCG GGC	GCA CGT A GTT CAA V	AAT TTA N 10 CAA GTT	CTT GAA L 070 GAG CTC	TTC AAG F  GGT CCA G	10: TCT AGA S	GGT CCA G 1080 CAA GTT Q	GAG CTC E	GGA CCT G GAA CTT E	GCT CGA A 109 GGA CCT G	CAA GTT Q 90 • GCT CGA	ACT TGA T CAA GTT Q	GCT CGA A 11 CAG GTC	CAG GTC Q 100 • CCA GGT	GCT CGA A> GCA CGT A>
N 100 GCA CGT A	CAA V 60 CCG GGC P	GCA CGT A GTT CAA V	AAT TTA N 10 CAA GTT Q	CTT GAA L 070 GAG CTC E	TTC AAG F GGT CCA G	TCT AGA S GTT CAA V	GGT CCA G 1080 CAA GTT Q	CAG GTC Q	GGA CCT G GAA CTT E	GCT CGA A 109 GGA CCT G	CAA GTT Q 90 GCT CGA A	ACT TGA T CAA GTT Q	GCT CGA A 11 CAG GTC Q	CAG GTC Q 1000 CCA GGT P	GCT CGA A> GCA CGT A>
TTA N 100 GCA CGT A	CAA V 60 CCG GGC P 1110	GCA CGT A GTT CAA V	AAT TTA N 10 CAA GTT Q GCA	CTT GAA L 070 GAG CTC E	TTC AAG F GGT CCA G	TCT AGA S GTT CAA V CAA	GGT CCA G 1080 CAA GTT Q 1	GAG CTC E CAG GTC Q	GGA CCT G GAA CTT E	GCT CGA A 109 GGA CCT G	CAA GTT Q 90 GCT CGA A 1140	ACT TGA T CAA GTT Q	GCT CGA A 11 CAG GTC Q	CAG GTC Q 100 CCA GGT P	GCA GCA GCA CGT A>
TTA N 100 GCA CGT A . CCT GGA	CAA V 60 CCG GGC P 1110 GCT CGA	GCA CGT A GTT CAA V	AAT TTA N 10 CAA GTT Q GCA CGT	CTT GAA L 070 GAG CTC E 11 CCT	TTC AAG F GGT CCA G	TCT AGA S GTT CAA V CAA GTT	GGT CCA G 1080 CAA GTT Q 1 GGC CCG	GAG CTC E CAG GTC Q	GGA CCT G GAA CTT E	GCT CGA A 10: GGA CCT G	CAA GTT Q 90 GCT CGA A 1140 TCT AGA	ACT TGA T CAA GTT Q	GCT CGA A 11 CAG GTC Q	CAG GTC Q 100 CCA GGT P 11:	GCA GCA GCA CGT A>

FIGURE 36 (3 of 4)

B-31 OSP B/ B-31 P41 (140 -295)

1170 1180 1190 1160 ACA ACT ACA GTT GAT GCT AAT ACA TCA CTT GCT AAA ATT GAA AAT GCT TGT TGA TGT CAA CTA CGA TTA TGT AGT GAA CGA TTT TAA CTT TTA CGA T T T V D A N T S L A K I E N A> 1230 1210 1220 ATT AGA ATG ATA AGT GAT CAA AGG GCA AAT TTA GGT GCT TTC CAA AAT TAA TCT TAC TAT TCA CTA GTT TCC CGT TTA AAT CCA CGA AAG GTT TTA IRMISDQRANLGAFQN> 1270 1260 1280 AGA CTT GAA TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA TCT GAA CTT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT R L E S I K N S T E Y A I E N L> 1320 1300 1310 AAA GCA TCT TAT GCT CAA ATA GGT CAC C TTT CGT AGA ATA CGA GTT TAT CCA GTG G K A S Y A Q I G H X>

Osp b/ fla (122-234) osp c Sequence Range: 1 to 1765

		. 10					20			30			4	C		
	•		•		•		•		•	•		•		•	•	
GCA	CAA	AA	A G	GT (	GCT	GAG	TCA	ATT	GGT	TCT	CAA	AAA	GAA	AAT	GAT	CTA
CGT	GTT	TT	rc	CA	CGA	CTC	AGT	TAA	CCA	AGA	GTT	111	CII	IIM	Cin	CAI
A	Q	ĸ		G	A	E	S	I	G	S	Q	K	E	×	D	L>
	-															
50				60			7	70			80		_	90		
•		•		•		•		•					•		~	- C1C
AAC	CTT	GA.	A C	SAC	TCT	AGT	AAA	AAA	TCA	CAT	CAA	AAC	GCT	***	CAA	CTC
TTG	GAA	CT	T C	TG	AGA	TCA	TTT	TTT	AGT	GTA	GTT	776	CGA	1	GII	D>
N	L	E		D	S	S	.K	K	S	н	Q	N	A	K	Ų	אמ
											1.	30		•	140	
10	00			1	.10			120			1.	•	•	•	•	
	•		•		•		CNC	תרא	CTC	тст	TTG	ттт	AAT	CGT	AAT	AAA
CIT	CCI	GC	G	STG	ACA	CTT	CTC	) CA	CYC	AGA	AAC	AAA	TTA	CCA	TTA	TTT
						E		VG.	v	S	L	F	N	G	N	K>
L	P	A	•	V	1	-		_	•							
	150				1 (	60			170			180			1	90
•		,		•		•	•		•		•	•		•		•
דדמ	רידים י	GI	`A	AGC	AAA	ĠAA	AAA	TAA	AGC	TCC	GGC	AAA	TAT	GAT	TTA	AGA
TAA	AAA	CA	T	TCG	TTT	CTT	TTT	TTA	TCG	AGG	CCG	TTT	ATA	CIA	AAT	TCT
	F	v	,	s	K	E	K	N	S	S	G	K	Y	כ	L	R>
									_							240
		200	)		•	210			2	20	_		230			240
•		•	•		•	•		•		•		. ===			,	- 3 T
GCA	AC	A AT	ĽΤ	GAT	CAG	GTT	GAA	CTI	· AAA	GG	ACT	700	CTA		77C	~~^
CGT					GTC	CAA	CTI	GAA	1111		TGA	י אטט	ν 714	· · · · ·	N.	N>
A	T	:	I	D	Q	V	E	L	K	G	•	. 3	D	••		
			2.5	. ^			260			270	3		2	38		
			25	•	•		•		•		•	•		•	•	
con	י דר	ጥ ር/	a.	ACC	CTI	GAZ	GGT	r TC	AA A	cc.	r GAC	AAC	AGT	LLA	GTA	AAA .
כסי	AG	A C	CT.	TGG	GAA	CT	CC	A AG	TT	C GG	A CTO	TTC	TCA	, <u></u>	CAT	TIT
G					L	E	G	s	K	P	D	K	s	7.	V	K>
-	_															
290				3,00	)	•		310			320			33(	)	
•		•		•	•	•		•		• .	•		•			- CAT
TT	A AC	A G	TT	TCI	r GC	r GA	T TT.	A AA	C AC	A GT	A AC	TT	A GAZ	4 GC	4 11. r hai	GAT
AA'	T TO						A AA	T TT	G TG	T CA	T TG	G AA	r Cr.	r ce X	I AA	CTA A
L	3	•	V	S	A	D	L	N	Т	ν	1	L	E	^	•	
					250			25	0			370			380	
	340		_		350		•	٥د	•	•		•		•	•	
				C 2 3	את ה	አ አጥ	ጥ ጥር	יא אי	44 T	A GT	T AC	T AA	A AA	A CA	G GG	G TCA
GC	CAC	,C A	MC TO	CT	ሌ ሌላ ጥጥ ጥ	ፈጥ ኤ ፕ	א אר	יר אני די דר	יי א	T C	A TG	A TT	T TT	T GT	c cc	C AGT
CG	۲۲ ي.	ل′ فار	16	. 01	,	* 13					, T	K	K	. 0	G	S>

FIGURE 37 (1 of 5)

Osp b/ fla (122-234) osp c

•	390		•	40	00	•	•	110		•	420		•	4:	30
ልጥል	ארא	GAG	GAA	ACT	רזיר	**	CCT	ልልሞ	AAA	ጥተኔ	CAC	ጥርኔ	220	8 3 B	- -
ጥልጥ	TCT	CTC	CTT	4OT	CAC	للملث	CCA	TTA	TTT	227	CTC	70-	TTC	744	TTA
ī	T	E	E	T	L	К	A	N		L	D	s	K		
•	•	~	_	•	-	•		••	•		D	3	~	K	L>
	4	440			450			4	60		4	470			480
•		•		•	•				•	•		•		•	•
									TAC						
TGT								CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
T	R	S	N	G	T	T	L	E	Y	S	Q	I	T	D	λ>
										± 1.5 1	•				
		49	90		5	500			510			52	20		
	•		ACA AAA TGT TTT			•		•	•		•		•	•	
											TTA	TCG	TAA	TTC	GAA
D	N	Α	T	K	A	v	E	T	L	K	N	S	I	K	L>
530			540			<b>E</b> 1	50			560					
220		•	240		•	5.	•		•	•			570		_
GAA	GGA	AGT	СТТ	ATD.	GTC	CCA	444	<b>ACA</b>	ACA	GTG	CAA	ት ጥጥ	,,,	~	~~
									TGT						
	G	S	L	v	v	G	ĸ	T	T	V	E	I	K	E	
_		_	-	•	•	•	••	•	•	•	L	•	V	-	G>
. 58	30		9	590			600			6:	Ö			520	
. 51	30 •	•	:	590		•	600		•	6:	0	•	6	520	
	•	• ACT		•	AGA	• GAA	•	GAA	• AAA		•			•	GTC
ACT	• GTT		СТА	AAA			ATT		AAA TTT	GAT	• GGA		GTA	AAA	
ACT TGA	• GTT		СТА	AAA TTT	TCT	CTT	ATT	CTT		GAT CTA	• GGA		GTA	AAA	
ACT TGA	GTT CAA V	TGA	CTA GAT	AAA TTT K	TCT R	CTT	ATT TAA I	CTT	TTT	GAT CTA	• GGA CCT G	TTT	GTA CAT	AAA TTT	CAG
ACT TGA	• GTT CAA	TGA	CTA GAT	AAA TTT K	TCT	CTT	ATT TAA I	CTT	TTT	GAT CTA	• GGA CCT	TTT	GTA CAT	AAA TTT	CAG V>
ACT TGA T	GTT CAA V 630	TGA T	CTA GAT L	AAA TTT K	TCT R 40	CTT E	ATT TAA I	CTT E 550	TTT	GAT CTA D	GGA CCT G	TTT	GTA CAT V	AAA TTT K	CAG V>
ACT TGA T	GTT CAA V 630	TGA T	CTA GAT L GAC	AAA TTT K 64	TCT R 40 • GCA	CTT E GGT	ATT TAA I TCT	CTT E 550 AAC	TTT K	GAT CTA D	GGA CCT G 660	TTT K GGT	GTA CAT V	AAA TTT K 67	CAG V>
ACT TGA T • TTT	GTT CAA V 630	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 • GCA CGT	E GGT CCA	ATT TAA I TCT AGA	E 50 AAC TTG	TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT	TTT K GGT CCA	GTA CAT V  AAA TIT	AAA TTT K 67 TGG ACC	CAG V> 0 GAA CTT
ACT TGA T	GTT CAA V 630	TGA T	CTA GAT L GAC	AAA TTT K 64 ACT TGA	TCT R 40 • GCA	E GGT CCA	ATT TAA I TCT	CTT E 550 AAC	TTT K AAA TTT	GAT CTA D	GGA CCT G 660	TTT K GGT	GTA CAT V	AAA TTT K 67	CAG V>
ACT TGA T • TTT	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 GCA CGT A	E GGT CCA	ATT TAA I TCT AGA	CTT E 550 * AAC TTG N	TTT K AAA TTT K	GAT CTA D	GGA CCT G 660 ACA TGT	TTT K GGT CCA G	GTA CAT V  AAA TIT	AAA TTT K 67 TGG ACC	CAG V> 0 GAA CTT E>
ACT TGA T • TTT	GTT CAA V 630 TTG AAC L	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 40 • GCA CGT	E GGT CCA	ATT TAA I TCT AGA	CTT E 550 * AAC TTG N	TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT	TTT K GGT CCA	GTA CAT V  AAA TIT	AAA TTT K 67 TGG ACC	CAG V> 0 GAA CTT
ACT TGA T TTT AAA F	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N	CTA GAT L GAC CTG D	AAA TTT K 6 ACT TGA T	TCT R 40 GCA CGT A 690	CTT E GGT CCA G	ATT TAA I TCT AGA S	CTT E 550 AAC TTG N	AAA TTT K	GAT CTA D • AAA TTT K	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V • AAA TTT K	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT E>
ACT TGA T TTTT AAA F	GTT CAA V 630 TTG AAC L	TGA T  AAT TTA N  680 ACT	CTA GAT L GAC CTG D	AAA TTT K 6 ACT TGA T	TCT R 40 GCA CGT A 690	CTT E GGT CCA G	ATT TAA I TCT AGA S	CTT E 550 AAC TTG N 70	AAA TTT K	GAT CTA D AAA TTT K	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT E> 720 AAA
ACT TGA T TTTT AAA F	GTT CAA V 630 TTG AAC L AGT TCA	TGA T  AAT TTA N  680 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690 TTA AAT	CTT E GGT CCA G	ATT TAA I TCT AGA S ATT TAA	E 550 AAC TTG N 70 AGT TCA	AAA TTT K	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V  AAA TIT K  AAA TIT	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT E> 720 AAA TTT
ACT TGA T TTTT AAA F	GTT CAA V 630 TTG AAC L	TGA T  AAT TTA N  680 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690	CTT E GGT CCA G	ATT TAA I TCT AGA S ATT TAA	E 550 AAC TTG N 70 AGT TCA	AAA TTT K	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G	GTA CAT V	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT E> 720 AAA
ACT TGA T TTTT AAA F	GTT CAA V 630 TTG AAC L AGT TCA	TGA T AAT TTA N 680 ACT TGA T	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 40 GCA CGT A 690 TTA AAT L	CTT E GGT CCA G	ATT TAA I TCT AGA S ATT TAA	E 550 AAC TTG N 70 AGT TCA	AAA TTT K	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	GGT CCA G 710 AAA TTT K	GTA CAT V  AAA TIT K  AAA TIT	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT E> 720 AAA TTT
ACT TGA T TTTT AAA F GAC CTG	GTT CAA V 630 TTG AAC L AGT TCA S	AAT TTA N 680 ACT TGA T	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 6 ACT TGA T ACT TGA T	TCT R 40 GCA CGT A 690 TTA AAT L	GGT CCA G ACA TGT T	ATT TAA I TAA I	AAC TTG N 70 AGT TCA S	AAA TTT K GCT CGA A	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T	GGT CCA G 710 AAA TTT K	GTA CAT V AAA TIT K AAA TIT K	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 0 GAA CTT E> 720 AAA TTT K>
ACT TGA T TTTT AAA F GAC CTG D	GTT CAA V 630 TTG AAC L AGT TCA S	AAT TTA N 680 ACT TGA T GTG	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 6 ACT TGA T ACT TGA T	TCT R 40 GCA CGT A 690 TTA AAT L	GGT CCA G ACA TGT T T 740 • GAT	ATT TAA I GGT	CTT E  550 AAC TTG N  70 AGT TCA S	AAA TTT K GCT CGA A 750	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	GGT CCA G 710 AAA TTT K	GTA CAT V AAA TIT K AAA TIT K CAA	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 0 GAA CTT E> 720 AAA TTT K>
ACT TGA T TTTT AAA F GAC CTG D	GTT CAA V 630 . TTG AAC L AGT TCA S TTG AAC	AAT TTA N 680 ACT TGA T 7: GTG CAC	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 6 ACT TGA T ACT TGA T	TCT R 40 GCA CGT A 690 TTA AAT L	GGT CCA G ACA TGT T T 740 • GAT	ATT TAA I GGT	CTT E  550 AAC TTG N  70 AGT TCA S	AAA TTT K GCT CGA A 750	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	GGT CCA G 710 AAA TTT K 7 CAA GTT	GTA CAT V AAA TIT K AAA TIT K CAA	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 0 GAA CTT E> 720 AAA TTT K>

89/133 Osp b/ fla (122-234) osp c 790 800 810 780 770 • • • ACA GCT GGA ACC AGC CTA GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TGT CGA CCT TGG TCG GAT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA T A G T S L E G S A S E I K N L> 850 840 830 820 TCA GAG CTT AAA AAC GCT TTA AAA GGT CAC CCC ATG GGA AAT AAT TCA AGT CTC GAA TTT TTG CGA AAT TTT CCA GTG GGG TAC CCT TTA TTA AGT S E L K N A L K G H P M G K N S> 880 890 900 • GGG AAA GAT GGG AAT ACA TCT GCA AAT TCT GCT GAT GAG TCT GTT AAA CCC TTT CTA CCC TTA TGT AGA CGT TTA AGA CGA CTA CTC AGA CAA TTT G K D G N T S A N S A D E S V K> 920 940 950 930 GGG CCT AAT CTT ACA GAA ATA AGT AAA AAA ATT ACG GAT TCT AAT GCG CCC GGA TTA GAA TGT CTT TAT TCA TTT TTT TAA TGC CTA AGA TTA CGC G P N L T E I S K K I T D S N A> 980 990 1000 970 GTT TTA CTT GCT GTG AAA GAG GTT GAA GCG TTG CTG TCA TCT ATA GAT CAA AAT GAA CGA CAC TTT CTC CAA CTT CGC AAC GAC AGT AGA TAT CTA V L L A V K E V E A L L S S I D> 1050 10 1020 1030 1040 GAA ATT GCT GCT AAA GCT ATT GGT AAA AAA ATA CAC CAA AAT AAT GGT CTT TAA CGA CGA TTT CGA TAA CCA TTT TTT TAT GTG GTT TTA TTA CCA E I A A K A I G K K I H Q N N G> 1070 1080 1090 TTG GAT ACC GAA TAT AAT CAC AAT GGA TCA TTG TTA GCG GGA CGT TAT AAC CTA TGG CTT ATA TTA GTG TTA CCT AGT AAC AAT CGC CCT GCA ATA L D T E Y N H N G S L L A G R Y>

1110 1120 1130

FIGURE 37 (3 of 5)

1130

GCA ATA TCA ACC CTA ATA AAA CAA AAA TTA GAT GGA TTG AAA AAT GAA CGT TAT AGT TGG GAT TAT TTT GTT TTT AAT CTA CCT AAC TTT TTA CTT A I S T L I K Q K L D G L K N E>

1140

Osp b/ fla (122-234) osp c 1170 1170 1180 1190 1160 • • GGA TTA AAG GAA AAA ATT GAT GCG GCT AAG AAA TGT TCT GAA ACA TTT CCT AAT TTC CTT TTT TAA CTA CGC CGA TTC TTT ACA AGA CTT TGT AAA G L K E K I D A A K K C S E T F> 1220 1210 1230 ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT CTT GGT AAA GAA GGT GTT TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA-GAA CCA TTT CTT CCA CAA T N K L K E K H T D L G K E G V>. 1270 1280 1260 ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA AAA ACA AAT GGT ACT AAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT TTT TGT TTA CCA TGA TTT T D A D A K E A I L K T N G T K> 1310 1320 1330 1300 ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT GAA TCA GTA GAG GTC TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT AAA CTT AGT CAT CTC CAG T K G A E E L G K L F E S V E V> 1360 1370 1380 TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAT TCA GTT AAA GAG CTT AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA TTA AGT CAA TTT CTC GAA L S K A A K E M L A N S V K E L> 1410 1420 1400 1430 ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA AAA CCT GGT ACC ATG GCT TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT TTT GGA CCA TGG TAC CGA T S P V V A E S P K K P G T M A> 1460 1470 1480 CAA TAT AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA AAT GTT ATA TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT TTA Q Y N Q M H M L S N K S A S Q N> 1520 1510 1500 GTA AGA ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT AAC ACA CAT TCT TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA TTG TGT V R T A E E L G M Q P A K I N T>

Osp b/ fla (122-234) osp c 1550 1560 1570 CCA GCA TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGA GTT CAT GGT CGT AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT TCT CAA GTA P A S L S G L Q A S W T L R V H> 1600 1610 1620 1590 GTT GGA GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT TAT GCA GCT CAA CCT CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA ATA CGT CGA V G A T Q D E A I A V N I Y A A> 1650 1660 1670 1650 1640 AAT GTT GCA AAT CTT TTC TCT GGT GAG GGA GCT CAA ACT GCT CAG GCT TTA CAA CGT TTA GAA AAG AGA CCA CTC CCT CGA GTT TGA CGA GTC CGA N V A N L F S G E G A Q T A Q A> 1720 1710 1690 1700 GCA CCG GTT CAA GAG GGT GTT CAA CAG GAA GGA GCT CAA CAG CCA GCA CGT GGC CAA GTT CTC CCA CAA GTT GTC CTT CCT CGA GTT GTC GGT CGT A P V Q E G V Q Q E G A Q Q P A> 1740 1750 1760 CCT GCT ACA GCA CCT TCT CAA GGC GGA GTT GGT CAC C GGA CGA TGT CGT GGA AGA GTT CCG CCT CAA CCA GTG G

PATAPSQGGVGHX>

		1	0			20			30		*	4	10	•	
OspC-B31 ATG	* AAA TTT				mm n	NOT.	CCC	ATE.	ጥጥል	ATG	ACT	TTA	TTT AAA	TTA AAT	TTT AAA
1. OspC-PK															
[ 1832 ]	•••	•••	•••	•••	•••	20	•••		30				10		
2. OspC-TR [ 1786 ]	• • •	•••	•••	•••	•••		•••	•••	•••	•••	•••	•••	•••	• • •	>
3. OspC-K4 [ 1774 ]	•••			•••	• • •	20 •••	•••	•••	30	•••	•••	•••	10	•••	>
50		*	60				70			80		*	90		•
	TCT	mam		3 3 70	TON	CCC	227	CAT	GGG	AAT TTA	ACA	TCT	GCA	AAT TTA	TCT AGA
1. OspC-PK50 [ 1832 ]	•••	•••	60 •g•	• • •	•••	•••	70	.g.		80 g	t	90	a.t	•••	c>
2. OspC-TR50			60			t	70 999	•••		tc.	80 g		a.t		0 >
3. OspC-K450 [ 1774 ]	•••	•••	60	•••	•••	t	70 999	•••		.cc	80 g	•••	a.t		90 >
	.00	_		110			120			1	30	*	:	140	
OspC-B31 GCT	GAT CTA	GAG CTC	TOT	CTT	מממ	CCC	CCT	TAA	CTT	ACA	GAA	ATA	AGT	AAA TTT	AAA TTT
1. OspC-100 [ 1832 ]															
2. OspC-TR [ 1786. ]		1	00	.ca	•••	110 a		•••	120	c	.t.		30 c		>
3. OspC-K4 [ 1774 ]	•••		00	.ca	•••	110 a			120	•••	.t.		30 c	•••	>
	150	<b>)</b>		1	60			170			180		•	19	90
OspC-B31 ATT	* DOA TGC	CAT	ጥርጥ	יייממ	GCG	CTT	ATT '	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG
1. OspC-PK150	) a			60	a	t	170 g			180	• • •	a	1	90 ••g	a.t>
2. OspC-T140 [ 1786 ]	a	٠	150	•	a	t	.60	9	•••	170	•••				t>
3. OspC-K140 [ 1774 ]	a	٠	150	• • • •	a	t	60 g	9	• • • •	170 . • • •	•••	a	180	g	t>
		200		*	210	)	*	2	20	4	•	230		*	240
OspC-B31 TTC	G CTC C GAC	TCA AGI	TCI AGA	מדמ י	GAT	GAA	ATI	GCT CGA	GCT	AAA TTI	GCT	ATI	GGT	AAA	AAA TTT
1. OspC-PK [ 1832 ]	200 . g.t	.t.	• • • •	210			. c.	20	aag		230	• • •		240 c	>
2. OSDC-TR	190			200			210	)			2	20			230 >

Figure 38 (1 of 3)

3. OspC-F	(4 19	0 a.c	•••	2	00	•••		210 c		aa.		0	•••	2	30	gt.>
OspC-B31	ATA TAT	CAC GTG	~~~	***	220	CCT	TTC	CAT	ACC	CAA	TAT ATA	AAT	CAC	AAT	GGA	TCA
1. OspC-1	ek	25 g	0 a.t	•••	2	60	a	.c.	270 g.t	tt.	a		g	•••	2	g>
						tac										
2 OanC-1	מיז			240		25	0		2	260			270			•
2. OspC-1	•••				g		а	•••	.a.	• • •	gca	• • •	.ga	с	.a.	>
3. OspC-I	<b>K4</b>	240			25	0	_	2	260	a +	aca	270		c	28	30
[ 1774 ]	•••	t	•••	•••	•••	• • •	a	<b>a</b>	y.c	a.c	geg	99.	•••	•••	•••	•••
	290			300			31	LŌ		:	320		_	330		
OspC-B31	* TTG AAC	ጥጥአ	CCC	CCA	CCT	ጥልጥ	CCA	ATA	TCA	ACC	CTA	ATA	AAA	CAA	AAA	TTA AAT
1. OsnC-i																
1. OspC-1 [ 1832 ]																
2. OspC-1	280	a	a	90	gc.	•••	300 .a.		•••	3: .aa	10	•••	.c.	320	•••	>
3. OspC-1	K4	:	290		acc	300			3.	10		3	320	g		330
[ 1//4 ]	• • •	• • •	a		guu	• • •	• • •							9		•
	, 34														380	
OspC-B31	CTA	40 # GGA CCT	TTG AAC	AAA TTT	AAT TTA	GAA CTT	* GGA CCT	360 TTA AAT	AAG TTC	* GAA CTT	AAA TTT	O * ATT TAA	GAT CTA	GCG CGC	380 # GCT CGA	AAG TTC
	GAT CTA	40 # GGA CCT	TTG AAC	AAA TTT	AAT TTA	GAA CTT	* GGA CCT	360 TTA AAT	AAG TTC	* GAA CTT	AAA TTT	O * ATT TAA	GAT CTA	GCG CGC	380 # GCT CGA	AAG TTC
1. OspC-	GAT CTA 340 ag.	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT 360	* GGA CCT	360 TTA AAT	AAG TTC	¢ GAA CTT 70 ac.	AAA TTT	ATT TAA	GAT CTA 380	GCG CGC	GCT CGA	AAG TTC
	GAT CTA 340 ag.	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT 360	* GGA CCT	360 TTA AAT	AAG TTC	¢ GAA CTT 70 ac.	AAA TTT	ATT TAA	GAT CTA 380	GCG CGC	GCT CGA	AAG TTC
1. OspC- [ 1832 ] 2. OspC- [ 1786 ]	GAT CTA 340 ag. TR330 ag.	GGA CCT	TTG AAC	AAA TTT 350	AAT TTA ttt	GAA CTT 360	* GGA CCT	360 TTA AAT	AAG TTC	¢ GAA CTT  70 ac.	37 AAA TTT 9 360	O * ATT TAA	GAT CTA 380 .ca	GCG CGC	GCT CGA	AAG TTC 390 >
1. OspC-	GAT CTA 340 ag. TR330 ag.	GGA CCT	TTG AAC	AAA TTT 350	AAT TTA ttt	GAA CTT 360	* GGA CCT	360 ** TTA AAT	AAG TTC	¢ GAA CTT  70 ac.	37 AAA TTT 9 360	O * ATT TAA	GAT CTA 380 .ca	GCG CGC	GCT CGA	AAG TTC 390 >
1. OspC- [ 1832 ] 2. OspC- [ 1786 ]	GAT CTA 340 ag. TR330 ag. K4	GGA CCT aa. .t.	TTG AAC	AAA TTT 350	AAT TTA ttt	GAA CTT 360 	* GGA CCT .a.	360 TTA AAT	AAG TTC 3 	GAA CTT 70 ac. a	3: AAA TTT g 360	70 * ATT TAA	GAT CTA 380 .ca a.a	GCG CGC	GCT CGA	AAG TTC 390>
1. OspC- [ 1832 ] 2. OspC- [ 1786 ]	GAT CTA 340 ag. TR330 ag. K4 ag.	aat. aa. TGT	TTG AAC	AAA TTT 350 t	AATTTA TTA ttt 	GAA CTT 360 	* GGA CCT	360 TTA AAT	AAG TTC 3 360 t	* GAA CTT 70 ac.	3: AAA TTT 360	70 * ATT TAA 3 420 GAA	GAT CTA 380 .ca a.a 70a	GCG CGC	GCT CGA	AAG TTC 390> 380>
1. OspC- [ 1832 ] 2. OspC- [ 1786 ] 3. OspC- [ 1774 ]	GAT CTA 340 ag. TR330 ag. K4 ag.	aa. .t. aa. 390	TTG AAC	AAA TTT 350 t	AAT TTA ttt a 40 tca ttc	GAA CTT 360  350 	* GGA CCT	360 TTA AAT	360 t	GAA CTT 70 ac. a	AAA TTT 9 360	70 * ATT TAA  3 420 GAA CTT	GAT CTA 380 .ca a.a 70 a	GCG CGC	GCT CGA	390>> 380>
1. OspC- { 1832 } 2. OspC- { 1786 } 3. OspC- [ 1774 } OspC-B31	GAT CTA 340 ag. TR330 ag. K4 ag.	aa. .t. 390	TTG AAC	AAA TTT 350 t 40 t	AATTTA ttta tca tca tca ACA	GAA CTT 360  350 	* GGA CCT	360 TTA AAT	360 t	GAA CTT 70 ac. a	AAA TTT	70 * ATT TAA  3 420 GAA CTT	GAT CTA 380 .ca a.a 70 a	GCG CGC aa. 3.a.	GCT CGA 70	390> 380> 360>
1. OspC- [ 1832 ] 2. OspC- [ 1786 ] 3. OspC- [ 1774 ] OspC-B31 1. OspC- [ 1832 ]	GAT CTA 340 ag. TR330 ag. K4 ag.	aa. .t. 390	TTG AAC	AAA TTT 350 t 40 t	AAT TTA ttt a 40 tca ttc a ACATGT ga.	GAA CTT 360  350 	* GGA CCT .aaag	360 TTA AAT	360  360 t	GAA CTT 70 ac. a TTA AAT 420	AAA TTT 360 	ATT TAA  3 420 GAA CTT	GAT CTA 380 .ca a.a 70 a AAA TTT 4	GCG CGC aa. .a. .a. cAC GTG	GCT CGA 70	AAG TTC 390> 380> 30 * GAT CTA>
1. OspC- { 1832 } 2. OspC- { 1786 } 3. OspC- [ 1774 } OspC-B31	GAT CTA 340 ag. TR330 ag. K4 ag. *AAA TTT	aa. .t. aa. 390 TGT ACA	TTG AAC	AAA TTT 350 t	AATTTA ttt a 40 tca ttc a ACA TGT ga.	GAA CTT 360  350 	* GGA CCT .aaag	360 TTA AAT 350	360 360 t 410	TTA	AAA TTT 360 	ATT TAA  420 GAA CTT agt	GAT CTA 380 .ca a.a 70 a AAA TTT 4	GCG CGC aa. 3.a. ca.	GCT CGA  70  4 ACA TGT	AAG TTC 390> 380> 380>
1. OspC- [ 1832 ] 2. OspC- [ 1786 ] 3. OspC- [ 1774 ] OspC-B31 1. OspC- [ 1832 ]	GAT CTA 340 ag. TR330 ag. K4 ag. * AAA TTT PK	aa. .t. 390 TGT ACA	TTG AAC	AAA TTT 350 t 40 t	AATTTAA tttta 40 ca ttca ACATGT ga. 390	GAA CTT 360  350  TTT AAA	* GGA CCT .aaag	360 TTA AAT 350 	360  360 t 410 AAA TTT	# GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA  3 420 GAA CTT agt	GAT CTA 380 .ca a.a 70 a AAA TTT 4 ggt	GCG CGC aa. .a. .a. cAC GTG	380 GCT CGA  70  4 ACA TGT 9 420 9	AAG TTC 390> 380> 380>

Figure 38 (2 of 3)

OspC-B31	CTT G	GT AA CA TT	A GAA CTT	GGT CCA	GTT CAA	ACT TGA	GAT CTA	GCT CGA	GAT CTA	GCA CGT	AAA TTT	GAA CTT	GCC CGG	ATT TAA	TTA AAT
1. OspC-Page 1832 ]				.a.	.c.		• • •	.a.	с	• • •	•••		t		
2. OspC-T															
3. OspC-4:	30	.a gt	440 t .ct	.c.	.c.	450	•••	.a.	c	•••	•••	•••	170 t	•••	>
		*	190		:	500		_	510			53	20		٠
OspC-B31	AAA A TTT T	CD DD	r com	DOT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	CTT	GGA	AAA	TTA
1. OspC-Pi [ 1832 ]	K 490	_	-	500		<b>~</b> 2	510			52	20	<b>t.</b> .	aa.	530 g.t	>
2. OspC-T	••••	c.	a	• • •	•••	gac	g	•••	•••	a	• • •	•••	.a.	g.g	>
3. OspC-K	4480		4	90		!	500			510	. C .		52	g - G	>
!	530 *	*	540 *		*	5	50 *	*	!	560 *		*	570 *		*
OspC-B31	TTT G	AA TC	A GTA I CAT	GAG CTC	GTC CAG	TTG AAC	TCA AGT	AAA TTT	GCA CGT	GCT CGA	AAA TTT	GAG CTC	ATG TAC	CTT GAA	CGA
1. OspC-P	K 5	40		59 a	50 .gt		.t.	560			570 c	.ta	gca	a	80 a>
					-								-		
2. OspC-5	20		530			540			5	50		!	560		
2. OspC-5 [ 1786 ]															
2. OspC-5 [ 1786 ] 3. OspC-K [ 1774 ]	4 53	0	• • • • •	540 a	ag.	•••	5! g.,	50	•••	g	660 C	a	gca ·	570 t.a	
3. OspC-K [ 1774 ]	4 53 .c 580	0	*	540 a 590	ag.	*	5! g 600	50	*	g	660 c	a	gca	570 t.a 520	>
3. OspC-K [ 1774 ] OspC-B31	4 53 .c 580	O 	* * T AAA	540 a 590 *	ag.	*	5! g., 600 *	SO	* GTT	g 6:	660 C LO *	a *	gca AGT	570 t.a 520 *	>
3. OspC-K [ 1774 ] OspC-B31	4 53 .c 580 * AAT T	CA GT	* T AAA A TTT	540 a 590 * GAG	ag. CTT GAA	* ACA	g 600 * AGC TCG	CCT GGA	* GTT CAA	g 6: GTG CAC	GCA CGT	a GAA CTT	gca AGT TCA	570 t.a 520 * CCA GGT	AAA TTT
3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	4 53 .c 580 ** ** ** ** ** ** ** ** ** ** ** ** **	CA GT GT CA	* T AAA A TTT	540 a 590 * GAG CTC	ag. CTT GAA 600	* ACA TGT	g 600 * AGC TCG	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 * CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	4 53 .c 580 ** ** ** ** ** ** ** ** ** ** ** ** **	CA GT GT CA	* T AAA A TTT	540 a 590 * GAG CTC	ag. CTT GAA 600	* ACA TGT	g 600 * AGC TCG	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 * CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]	580 AAT T TTA A K 	CA GT CA	* T AAA A TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	580 AAT T TTA A K 	CA GT CA	* T AAA A TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]	580 580 AAT T TTA A K 	CA GT CA	* T AAA A TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]	580 AAT T TTA A K R570 4	CCA GT GT CA 590	* AAAA TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]	580 AAT TTA A K 4 4 K TTT G X X X X X X X X X X X X X X X X X X X	CA GT CA 590	* AAAA TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P	580 AAT TTA A K R570 4 AAA C TTT G	CCA GT GT CA 590 580 580 CT TA	* AAAA TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630
3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T	580 AAT TTA A  K 4 AAA C TTT G  K R 62	CCA GT GT CA 590 580 580 CT TA	* AAAA TTT	540 a 590 * GAG CTC	CTT GAA	* ACA TGT	9 600 * AGC TCG t	CCT GGA	GTT CAA	63 GTG CAC	GCA CGT	GAA CTT	gca AGT TCA	570 t.a 520 CCA GGT	AAA TTT 630

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_	<b>-</b> ,	, GAT	CCA	CTT	AAT	TTA	GTC	GAT	AAC	CCC	GTT	TGA	TGT	TIM	MGI	GAI	111
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ı	2786 ]	·				•••	· • • •	• •	• • • •		•••	• • • •	• • •	• • • •	• • •	• • •	>
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_	202	777	* 	* *	ימט ג	*	لىنلىن بە	ነ ጉ ይጥ:	≄ ימג ג	r Gጥር	* 3 GT'	* רממים	TT!	. = \ ATI	TC	TC	T GCT
1	30 ospD	AAA TT:	r CAI	A CAT	CT	r CGT	CAI	TA	T TC	A CAC	CA	A TT	AA A	TAT 1	AG:	r AG	A CGA

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1. P-Gau	۰ .	200		210			22	20		2	230	•		240
1. P-Gau	•••	• • • • •	•••		• • •	•••	•••	•••	• • •	•••	•••	•••	•••	>
2. DK29 c	8	200		210			22	20		2	230			240
2. DK29 c [ 2786 ]	•••	• • • • •	• • • • •	• • • •	• • •	••••	• • •	•••	•••	• • •	• • •	• • •	•••	>
3. K48 os	1D	200		210			22	20		2	230			240
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1								270			20			
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BO ospD	GCA GA	T CAG	GTA AA	A GGT	CAA	CAA	CAA	ATA	TGC	ACG	ATT	TAG	CTC	AAA
-	CGT CI	A GTC	CAT TT	T CCA	GTT	GTT	GTT	TAT	ACG	TGC	TAA	ATC	GAG	TTT
1. P-Gau [ 2804 ]	•	29	50	:	260			270			28	30		
[ 2804 ]	•••	• •••	•••	• • • •	• • •	•••	• • •	• • •	• • •	• • •		•••	•••	>
2. DX29 c	8	29	50	:	260			270			28	30		
[ 2786 ]	•••		g		• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••	>
3. K48 os	in ·	20	50	•	260			270			28	30		
3. K48 os [ 2786 ]	··· · · ·	· · · · ·	g		•••	• • •		•••	• • •	• • •	•••	• • •		>
	290 *		300		3:	10		:	320			330		
D0D	*	*	*	*		*	*	200	*	C/T/N	*	* 7077	220	# ሞአካ
BO ospD	TGG CA	G AAA	TAG AT	T TAG A ATC	TTT	TTT	ATT	TCC	TTA	GAT	CAC	TAT	TTC	ATT
1. P-Gau [ 2804 ]	290		300		3.	10			320			330		>
•														
2. DK29 c	290		300		3:	10			320			330		_
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3. K48 of	290		300		3	10		;	320			330		_
[ 2786 ]	•••	• • • •	•••	• • • • •	•••	• • •	• • •	• • •	• • •	• • •	•••	•••	•••	>
	340		350			360			37	70			380	
	*		350 *											
BO ospD	TAG T	rg cgg	CTA AT	G TTG	CGA	AAG	AAG	CAT	ATA	ACC	TTA	CTA	AAG	CAG
	ATC A	AC GCC	GAT TA	C AAC	GCT	TTC	TTC	GTA	TAT	TGG	AAT	GAT	TTC	GTC
1. P-Gau			350						31	70			380	
[ 2804 ]	•••	• • • • •	•••	• • • •	• • •	• • •	• • •	•••	• • •	•••	• • •	• • •	•••	>
2. DK29 d	эв 340		350	·		360			31	70		:	380	
[ 2786 ]	• • • •				• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	• • •	>
3. K48 o	340		350	)		360			3:	70		:	380	
[ 2786 ]													• • •	>
		90	*	400			410			420			4:	30
BO ospD														
nd oahn			TAT AC											
1 D_C		20		400			<i>4</i> 10			420			4:	30
1. P-Gau [ 2804 ]	0 3													
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2. DK29	os 31	90		400			410			420			4.	30

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	3. K48 os 2786 ]	q	390			4	00			410		•••	420	•••	•••	4:	30
		*		440		*	450		*	4	60 *	*		470 *		ŧ	480
В	O ospD	AAC TTG				TTC	TGA	TGA	AAC	AGA	ACG	AGT	TTC	TGA	TGA		
	1. P-Gau 2804 ]				•••	•••	450 •••	•••	•••	4		•••		470 •••	•••		480 >
ι	2. DK29 o 2786 ]			440	•••	•••	450 •••		.g.	40	50 •••	•••	•••	470 •••	•••	•••	480
_	3. К48 ов	P		440			450			40	50			470			480
τ	2786 ]	•••	• • •	• • •	• • •	•••	•••	•••	·g·	•••	•••	•••	•••	•••	•••	• • •	>
			*	49	90	*	:	500		*	510		*	52	20	*	
В	Oqao O	ACA TGT	AGC TCG	TAA ATT	AGA TCT	CCG	TGT ACA	AGA TCT	AAT TTA	AGC TCG	TTG AAC	GAA CTT	AGC TCG	CAC GTG	AGT TCA	AAA TTT	AGT TCA
E	1. P-Gau 2804 ]	• • • •	•••	49	90	•••		500	•••	•••	510	•••	•••	52	20	•••	>
ι	2. DK29 o 2786 ]	s •••	• • •	49	90	•••	•••	•••	•••	•••	510	•••	• • •	52	20	•••	>
Į	3. K48 os 2786 ]	P 	• • •	49	90	•••			•••	•••	510	•••	• • •		20	•••	>
		530 *		*	540		*	5!	50	*	!	560		*	570		
B	O ospD	AAA TTT	AGA	TGA	GTT	AAT	TGA	TGT	AGA	AAA	TGC	AGT	CAA	AGA	GGC	ATT	GGA
r	1. P-Gau 2804 }	530			540			5!	50		!	560			570		
١	2. DK29 o															•••	•••>
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(	3. K48 os 2786 ]		• • •		540		•••		50			560	•••	•••	570	•••	>
			30	•		90			600			61	10		•	520	
В	O ospD	TAA	AAT	AAA	GAC	AGA	AAC	CGC	GAA	CAA	TAC	AAA	ACT	TAC	AGA TCT	TAT	aga TCT
	1. P-Gau ( 2804 ]			•••		90	•••	•••	600			61		•••		520	>
£	2. DK29 of 2786 ]	s 58		•••		90	•••	•••	600		•••	61		•••		520	>
f	3. K48 os; 2786 ]	p 58	30	•••		g	•••	•••	600	•••	•••	61		•••		520	>

									9	8/13	3.3						
		630		*	64	*	*		550 *	•	*	660 *		*	67	*	
BO ospD	202	AGT TCA	AGC TCG	AGA TCT	GTT CAA	AGT TCA	ATT TAA	ACA TGT	GAT CTA	AGC TCG	CAA GTT	AAA TTT	TGT ACA	AGC TCG	GGA CCT	AAT TTA	
1. P-Gau (	•	630		•••	64	40	•••		650 a	•••	•••	660	•••	•••	67	70 >	
2. DK29 of [ 2786 ]	в	630	•••	•••	64	<b>4</b> 0	•••	•••	650 a	•••	•••	660	•••	••••	67	70 >	
3. K48 os [ 2786 ]	P	630	•••	•••		40	•••	• • •	650 a	•••	•••	660	•••	•••		70 >	
		1	680			690			7	00							
BO ospD	* AGC TCG	GCA CGT	# AGA	AGT TCA	# TGT ACA	GGC CCG	CTT GAA	* GTT CAA	AAA TTT	* TAC ATG	TT AA						
1. P-Gau [ 2804 ]	o 	•••	680	•••	•••	690			7	00	>						
2. DK29 o [ 2786 ]	8	• • •	680	•••	•••	690		•••		00	>						
3. K48 ов [ 2786 ]	P				• • •	690			7	00	>						

P41 Sequence Range: 1 to 1011 10 20 ATG ATT ATC AAT CAT AAT ACA TCA GCT ATT AAT GCT TCA AGA AAT AAT TAC TAA TAG TTA GTA TTA TGT AGT CGA TAA TTA CGA AGT TCT TTA TTA Met Ile Ile Asn His Asn Thr Ser Ala Ile Asn Ala Ser Arg Asn Asn> 80 90 70 60 50 GGC ATT AAC GCT GCT AAT CTT AGT AAA ACT CAA GAA AAG CTT TCT AGT CCG TAA TTG CGA CGA TTA GAA TCA TTT TGA GTT CTT TTC GAA AGA TCA Gly Ile Asn Ala Ala Asn Leu Ser Lys Thr Gln Glu Lys Leu Ser Ser> 130 120 110 100 GGC TAC AGA ATT AAT CGA GCT TCT GAT GAT GCT GCT GGC ATG GGA GTT CCG ATG TCT TAA TTA GCT CGA AGA CTA CTA CGA CGA CCG TAC CCT CAA Gly Tyr Arg Ile Asn Arg Ala Ser Asp Asp Ala Ala Gly Met Gly Val> 170 180 190 150 160 TCT GGT AAG ATT AAT GCT CAA ATA AGA GGT TTG TCA CAA GCT TCT AGA AGA CCA TTC TAA TTA CGA GTT TAT TCT CCA AAC AGT GTT CGA AGA TCT Ser Gly Lys Ile Asn Ala Gln Ile Arg Gly Leu Ser Gln Ala Ser Arg> 220 230 210 AAT ACT TCA AAG GCT ATT AAT TTT ATT CAG ACA ACA GAA GGG AAT TTA TTA TGA AGT TTC CGA TAA TTA AAA TAA GTC TGT TGT CTT CCC TTA AAT Asn Thr Ser Lys Ala Ile Asn Phe Ile Gln Thr Thr Glu Gly Asn Leu> 280 260 270 250 AAT GAA GTA GAA AAA GTC TTA GTA AGA ATG AAG GAA TTG GCA GTT CAA TTA CTT CAT CTT TTT CAG AAT CAT TCT TAC TTC CTT AAC CGT CAA GTT Asn Glu Val Glu Lys Val Leu Val Arg Met Lys Glu Leu Ala Val Gln> 320 300 310 290 TCA GGT AAC GGC ACA TAT TCA GAT GCA GAC AGA GGT TCT ATA CAA ATT AGT CCA TTG CCG TGT ATA AGT CTA CGT CTG TCT CCA AGA TAT GTT TAA Ser Gly Asn Gly Thr Tyr Ser Asp Ala Asp Arg Gly Ser Ile Gln Ile> 370 360 340 350 GAA ATA GAG CAA CTT ACA GAC GAA ATT AAT AGA ATT GCT GAT CAA GCT

FIGURE 40 (1 of 3)

CTT TAT CTC GTT GAA TGT CTG CTT TAA TTA TCT TAA CGA CTA GTT CGA Glu Ile Glu Gln Leu Thr Asp Glu Ile Asn Arg Ile Ala Asp Gln Ala>

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•	•		C	<b>&gt; T</b>	•	• •	ጥፒክ '	TCA	220	AAA	TCT -	CCT	ىنى 	C32	227
CAA	TAT	TTG	CAN	TAC	CAC .	MIG MIG	TAA	AGT	TTG	TTT	AGA	CGA	AGA	GTT	TTA
Gln	TVI	Asn	Gln.	Met	His 1	Met	Leu	Ser	Àsn	Lys	Ser	Ala	Ser	Glm	ลรก>
02	-3-									_					
	4	40			450			46	0		4	70			480
•		*		•	•		•		•	•		•		•	•
GTA	AGA	ACA	GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	AAA	ATT	AAC	ACA
CAT	TCT	TGT	CGA	CTT	CIC	GAA	CCL	TAC	GIC	GGA	rol.	TVC	TIA	116	Thr>
vai	Arg	inr	Ald	GIU	GIU	Leu	GLY	Mec	G111	110	AZG	Ly S	116	VOII	:111.
		49	90		5	00			510			52	20		
	•		*	•		•		•	•		*		•	•	•
CCA	GCA	TCA	CTT	TCA	GGG	CTT	CAA	GCG	TCT	TGG	ACT	TTA	AGA	GTT	CAT
GGT	CGT	AGT	GAA	AGT	CCC	GAA	GTT	CGC	AGA	ACC	TGA	TAA	TCT	CAA	GTA
Pro	Ala	Ser	Leu	Ser	Gly	Leu	Gln	Ala	Ser	Trp	Thr	Leu	Arg	Val	His>
530			540			55	0			560			570		
530		•	540		•	. د	•	•	•	*		•	•		•
GTT	GGA	GCA	ACC	CAA	GAT	GAA	GCT	ATT	GCT	GTA	AAT	ATT	TAT	GCA	GCT
										CAT					
Val	Gly	Ala	Thr	Gln	Asp	Glu	Ala	Ile	Ala	Val	Asn	Ile	Tyr	Ala	Ala>
			_							٠,					
58	30		:	590			600		•	61	•	•		£29 •	
יי א א	CAAL _	GC.	דבב	CTT	ттс	TCT	GGT	GAG	GGÀ	GCT	CAA	ACT	GCT	CAG	GCT
										CGA					
															Ala>
	630		_	. 64	40		•	550		_	660			€.	70
	•	<del>ር ጥ</del> ጥ	C	CAG	CCT	CTT -	CLA	CAG	GAA	GGA	CCT.		CžG	CC3	GC.
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		680			690			7	00			710			725
•		•		•	mcm	C	•	CC3	- COM	• • * * * •	TCT.	•	C TT	•	- -
										TAA '					
Pro	Ala	Thr	Ala	Pro	Ser	Gln	Gly	Gly	Val	Asn	Ser	Pro	Val	Asn	Val>
							_	-							
		7	30		•	740			750	)		7	60		
	•		•	•		•		*	•		•		•	•	
										GCT					
															CGA Alax
1111		. 1111	. val	, voh	, via	noll		Jer	Dec	. 417	. Dy c		. 510		
770			780	)		7	90			800			810	)	•
•		•	•		•		•	•	•	•		•	•	,	•
										ATT 1					
															י ידה
			. 11/	COV	- Acr	i Glr	Arc	, Ala	a Asi	n Lei	ı Gl\	/ Ala	a Phe	e Gir	: Asn>

830 840 850 860 820 AGA CTT GAA TCT ATA AAG AAT AGT ACT GAG TAT GCA ATT GAA AAT CTA TCT GAA CTT AGA TAT TTC TTA TCA TGA CTC ATA CGT TAA CTT TTA GAT Arg Leu Glu Ser Ile Lys Asn Ser Thr Glu Tyr Ala Ile Glu Asn Leu> 870 880 890 900 AAA GCA TCT TAT GCT CAA ATA AAA GAT GCT ACA ATG ACA GAT GAG GTT TTT CGT AGA ATA CGA GTT TAT TTT CTA CGA TGT TAC TGT CTA CTC CAA Lys Ala Ser Tyr Ala Gln Ile Lys Asp Ala Thr Met Thr Asp Glu Val> 930 940 " 920 960 GTA GCA GCA ACA ACT AAT ATG ATT TTA ACA CAA TCT GCA ATG GCA ATG CAT CGT CGT TGT TGA TTA TAC TAA AAT TGT GTT AGA CGT TAC CGT TAC Val Ala Ala Thr Thr Asn Met Ile Leu Thr Gln Ser Ala Met Ala Met> 990 980 970 1000 ATT GCG CAG GCT AAT CAA GTT CCC CAA TAT GTT TTG TCA TTG CTT AGA TAA CGC GTC CGA TTA GTT CAA GGG GTT ATA CAA AAC AGT AAC GAA TCT Ile Ala Gln Ala Asn Gln Val Pro Gln Tyr Val Leu Ser Leu Leu Arg> 1010 TAA ATT

FIGURE 40 (3 of 3)

#### Alignment List

Search from Date: Octob	Search Analysis for Sequence: B31-41kD Search from 1 to 1011 where origin = 1 Date: October 22,1993 Time: 15:03:24  Matrix: DNA database matrix Score Region from 1 to 1011 Maximum possible score: 4044															
Database: U	serFo	lder	: 41	kD	Flag	elli	n cl	ones	•							
)			1	0	*		20		*	30 *	•	*	4	0	*	
B31-41kD	ATG TAC	ATT	ATC	AAT	CAT	TAA	ACA	TCA	GCT	TTA	TAA	GCT	TCA	AGA TCT	AAT TTA	AAT ATT
1. KA-41k [ 3996 ]		•••					20					•••		0	•••	>
2. P-Gau- [ 3696 ]	4	•••	1	0		•••	20 	•••		30		•••		0	•••	>
3. BO-41k	D			.0		•••	20			30	•••			0		>
4. DK29-4 [ 3672 ]															•••	>
5. PKO-41 [ 3672 ]															• • •,	>
·	50		_	60				70	_		80		_	90		_
B31-41kD		TTA AAT	AAC TTG	GCT	GCT	AAT	CTT	AGT	AAA	ACT	CAA	GAA	AAG	CTT	TCT	AGT TCA
1. KA-41k [ 3996 ]	:D50			60				70 	•		80		• • •	90		>
2. P-Gau- [ 3696 ]	450 .c.	• • •	t	60	•••	•••		70		с	80	g		90		>
3. BO-41) [ 3684 ]			t									g			•••	>
4. DK29-4	150 t	•••	t	60	•••	•••	•••	70		•••	80					>
5. PKO-41			t	60		•••		70 		c	80	g	•••	90 .c.	•••	>
	10	00	•		110		,•	120		*	1	30			140	
B31-41kD	CCC	TAC	AGA TCT	TTA KAT	TAA T	CGA	GC1	ו זכז	GAT	GAT CTA	GCT CGA	GCT CGA	GGC	ATG TAC	GGA	GTT CAA

	*			
1. KA-41kD 100 [ 3996 ]g	110	120	130	140
2. P-Gau-4 100 [ 3696 ]t	110	120	130	140 tg>
3. BO-41kD 100 [ 3684 ]t	110	120	130	140 tg>
4. DK29-41 100 [ 3672 ]t	110 a.	120	130	140 tg>
5. PKO-41k 100 [ 3672 ]t	110		130	140 tg>
150	160	170	180	190
B31-41kD TCT GGT AGA CCA	AAG ATT AAT GO TTC TAA TTA CO	T CAA ATA AGA A GTT TAT TCT	GGT TTG TCA CCA AAC AGT	CAA GCT TCT AGA GTT CGA AGA TCT
1. KA-41kD 150 [ 3996 ]				
2. P-Gau-4 150 [ 3696 ]c	••• ••• •••	c.	ca	
3. BO-41kD 150 [ 3684 ]c	160	170	180 ca	190
4. DK29-41 150 [ 3672 ]g	160	170	180 a	190
5. PKO-41k 150	160	170	180	190
	200 2	210	220	230 240
777 411cm 77 7CT	י יירא אום כרייי ז	TT AAT TTT AT	CAG ACA ACA	
1. KA-41kD [ 3996 ]	200	210	220	230 240>
2. P-Gau-4 [ 3696 ]c	200 :	210 c	220	230 240 a>
3. BO-41kD [ 3684 ]c	200			230 240 240
4. DK29-41 [ 3672 ]c	200	210	220	230 240
5. PKO-41k [ 3672 ]c	200	210	220	230 240

							•									
			25		•	2	260 *		•	270		*	28	30	*	
B31-41kD	AAT (	GAA CTT	GTA CAT	GAA CTT	AAA TTT	GTC CAG	ATT TAA	GTA CAT	AGA TCT	ATG TAC	AAG	GAA CTT	TTG AAC	GCA CGT	CAA	CAA GTT
`1. KA-41k	D CL		25	50		2	260			270			28			
[ 3996 ]	• • •	• • •	• • •	•••	• • •	•••	• • •	• • •	• • •	• • •	•••	•••	•••	•••	•••	>
2. P-Gau- [ 3696 ]	4			50		t	260	• • •	• • •	270 	a		28 a	30	•••	>
3. BO-41) [ 3684 ]	æ	• • •	25	50		t	260		•••	270	a	•••	.28 a	30	•••	>
4. DK29-4	•••			•••	•••	t	•••	• • •	•••		á	·	a	•••	•••	>
5. PKO-41	.k		25	50		:	260	•		270			28	30		
[ 3672 ]	•••	• • •	•••	•••	•••	t	• • •	•••	• • •	• • •	a	•••	a	•••	•••	>
	290			300			3:	10		-	320		<b>±</b>	330		*
B31-41kD	TCA AGT	GGT	AAC	GGC	ACA	TAT	TCA	GAT	GCA	GAC	AGA	GGT	TCT	ATA	CAA	ATT
1. KA-41)	290			300			3:	10		3	320			330		
[ 3996 ]	• • •	• • •	•••	•••	• • •	•••	•••	• • •	•••	• • •	•••	• • •	• • •	• • •	• • •	>
2. P-Gau-				300			3:	10			320			330		
[ 3696 ]													•••	• • •	g	>
3. BO-411 [ 3684 ]														330	g	>
4. DK29-							3									
[ 3672 ]	• • •	• • •														
5. PKO-4:															σ	
					,				•	•••	•••	•••	•••	•••	•••	
•	34	0			350			360			3	70	•	:	380	
B31-41kD	GAA															GCT
	CTT	TAT	CTC	GTT	GAA	TGT	CIG	CTT	TAA	TTA	TCT	TAA	CGA	CTA	GTT	CGA
1. KA-41 [ 3996 ]	kD 34	_						360		•••	3	70 			380	>
2. P-Gau					350							70			380	
[ 3696 ]	• • •	• • •	• • •	•••	• • •	•••	• • •	• • •	•••	•••	•••	• • •	• • •	•••	g	···>
3. BO-41 [ 3684 ]								360					• • •		380 ••g	>
4. DK29-	41 34	0			350			360	١		3	70			380	

	•								,,,	_							
I	3672 ]	•••	•••	• • •	•••	•••	•••	• • •	• • •	•••	•••	• • •	•••	• • •	• • •	•••	>
	5. PKO-413 3672 ]	34	10		3	50			360			37	0		3	80	
ı	36/2 ]	• • •	•••	•••	•••	•••	•••	•••	• • •	•••	•••	•••	•••	•••	•••	••9	• • • •
			390		•	40	00		4	10		*	420		*	43	0
B	31-41kD	CAA	TAT	AAC	CAA	ATG	CAC	ATG	TTA	TCA	AAC	AAA	TCT	GCT	TCT	CAA GTT	AAT
ſ	1. KA-41kI 3996 <sub>2</sub> ]	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••.	•••	•••	• • •	• • •	• • •		>
ſ	2. P-Gau-4	4	390	• • •	•••	40		•••	g	110	:	₹	420	•••	c	43	0
I	3. BO-41ki 3684 }		390		•••	40		•••	g	110	•••	•••	420	•••		43	
I	4. DK29-43 3672 ]	1	390	• • •		40			g	410	•••		420		c	43	0
Į	5. PKO-411 3672 ]	k 	390	• • •	···	41	00		g	410	•••	•••	420	•••	с	43	0
		*	•	440			450			4	60 *	•	4	170 *		•	480
B	31-41kD															AAC	
I	1. KA-41ki 3996 ]	D 	• • •	440	•••		450 			4	60	•••		470 • • • •	• • •	• • •	480 >
1	2. P-Gau-	4	.a.													•••	
I	3. BO-41k 3684 )	D 	.a.	440	•••	•••	450 			4	60 	•••	• • •	470 •••			480 >
	4. DK29-4 3672 ]														c		480 >
ſ	5. PKO-41 3672 ]	k 		440	•••	•••	450 		•••		60 	•••	•••	470 	•••	•••.	480 >
			*	4	90	*		500		•	510		*	5	20	•	
B	31-41kD															GTT CAA	
Į	1. KA-41k 3996 }							500 tc.		· • • •	510				20	•••	>
I	2. P-Gau- 3696 ]	·4 · · ·			190		a	500 tc.		t	510				20		>

ſ	3. BO-41kD	) 	• • •	49	0	•••	a	00 tc.	• • •	t	510				0	•••	>
I	4. DK29-41 3672 }	•••	g	49	0		a	00 tc.		t	510		•••	52			>
I	5. PKO-41k	: 		49	0		a	00 tc.	•••	t	510	•••	•••	52		• • •	>
	* <sub>V</sub> -5	30			540			55	50		5	60			570		
B	31-41kD	GTT CAA	GGA	GCA	ACC	CAA	GAT	GAA	GCT	ATT	GCT CGA	GTA CAT	TAA ATT	TTA	TAT	GCA	
I	1. KA-41k5 3996 ]	30			540 .a.		• • •	55	50		5	60		•••	570	• • •	>
I	2. P-Gau-5	30 g			540 .at			55	50 a			60		•••	570	t	>
ſ	3. BO-41k5														570	t	>
I	4. DK29-45	g			540 .at			5:	50 g			60		•••	570		>
	5. PKO-415														570	t	>
		58	30		5	590			600			61	.0		•	520	
B	31-41kD		GTT	GCA	TAA	CTT	TTC	TCT	GGT	GAG	GGA	GCT	CAA	ACT	GCT	CAG	
	1. KA-41ki 3996 ]																>
	2. P-Gau-4 3696 ]																>
1	3. BO-41ki 3684 ]	D 58	30		:	590		_	600			61	10	_	•	520	>
	2004 ]	• • •	• • •	• • •	•••	• • •	٠.٠	9	• • •	• • •	• • •	• • •	• • •	g	• • •	• • •	
L	4. DK29-4				!	590			600			6:	10		(	520	
	4. DK29-4	1 58	30			590 a 590	•••	•••	600	a	•••	6:	10 g	g	•••	520 	-
	4. DK29-4 3672 ] 5. PKO-41	1 58  k 58	30	•••		590 a 590 	•••	•••	600	a	•••	6:	10 g	g	•••	520 	a>

		•															
[	1. KA-41kI 3996 ]	•••	630		•••	64	10	•••		650	•••		660	•••	•••		70 •••>
	2. P-Gau-4															6	
	3. BO-41kI 3684 ]																
	4. DK29-41 3672 ]														a		70 >
	5. PKO-41)	ς .	630			64	10		(	650			660			6.	70
				680			690			70	00			710			720
B	31-41kD	CCT GGA	GCT CGA	* ACA TGT	GCA	CCT	TCT	CAA	GGC	GGA	GTT	AAT	TCT	CCT	GTT CAA		GTT CAA
	1. KA-41kI 3996 ]	)	(	680			690			70	00			710			720
	2. P-Gau-4	1	(	680			690			70	00			710			720
I	3. BO-41kI							•••	t	70	00	•••		710	•••		720 >
I	4. DK29-43	١		680	g	•••	690	9	t	7(	00			710			720
	5. PKO-41)	ς.		680			690			7(	00		•	710			720
	•				30			740								•••	
В3	31-41kD	ACA	ACT	ACA	*	* GAT	GCT	* AAT	ACA	TCA	CTT	GCT	* AAA	ATT	GAA	Aat	GCT
	1. KA-41ki 3996 ]															TTA	
	2. P-Gau-6												•••	a	•••	•••	>
	3. BO-41ki 3684 )					•••	•••	740	•••	• • • • •	750 	• • •	•••	76 a	50	•••	>
	4. DK29-4: 3672 ]				30			740			750 			76 a	50	•••	>
	5. PKO-411 3672 }			7				740	•••		750			76 a			>

					, ,	9//3	3.2							
	770	•	780	•	79	0	•	. 8	00	•	<b>.</b>	810		•
B31-41kD	ATT A	AGA ATG	ATA AGT	GAT CTA	CAA GTT	AGG TCC	GCA CGT	TTA .	ATT TAA	CCA	GCT CGA	TTC AAG	CAA GTT	TTA ATT
1. KA-41	k770		780		79	0		8	00			810		
[ 3996 ]	•••			• • •	•••	• • •	• • •	• • •		• • •	• • •	• • •	• • •	>
2. P-Gau [ 3696 ]	-770		780	•••	79 • • •	0 a			00	•••	•••	810	•••	>
3. BO-41 [ 3684 ]	k770	••••	780	•••		a		•••	•••	•••	•••	810	•••	>
4. DK29-	4770		780		. 79	0			00 ~			810		
[ 3672 ]	•••	•••	•••	• • • •	•••	a	•••	• • •	•••	• • •	•••	•••	• • •	>
5. PKO-4	1770		780		79	90		8	00			810		
[ 3672 ]	•••	• • • • • •	•	• • • •	•••	a	•••	•••	•••	•••	•••	• • •	• • •	>
	82	0 .	830			840			85	50	*	8	360	
B31-41kD	AGA	CTT GAA	TCT AT	A AAG	AAT	AGT	ACT	GAG	TAT	GCA	ATT	GAA	AAT	CTA
	TCT	GAA CTI	' AGA TA	r Trc	TTA	TCA	TGA	CIC	ATA	CGT	TAA	CIT	TIA	CAT.
1. KA-41 [ 3996 ]	kD 82	0	830			840	• • •			50			360	>
2. P-Gau	4 00		020			040			Q	50		•	360	
[ 3696 ]		••••			• • •	0	• • •	• • •	•••	t	•••	•••	•••	>
3. BO-41 [ 3684 ]	kD 82	:0	830			840	ı		8	50		1	360	
[ 3684 ]	• • •	• • • • •		• • • • •	•••		• • • •	• • •	•••	t	•••	• • •	• • •	>
4. DK29- [ 3672 ]	-41 82	20	830		a	840	)		8	50 t		1	860	>
5. PKO-4	11k 82	20	830	• •••	•••	840	) :	•••	8	50 t		• • •	860 •••	>
		970		990			890			900			c	10
			*											
B31-41kD	AAA TTT	GCA TC	T TAT GO A ATA CO	T CAA SA GTT	ATA TAT	AAA TT	GAT CTF	GCT CGA	ACA TGI	OTA C	ACA TG1	GAT CTA	CTC	CAA
1. KA-4	1kD	870		880			890			900	)		9	10
[ 3996 ]									•••			• • • •		>
2. P-Ga				880			890			900				910
[ 3696 ]	• • •	•••	• • • • •	• • • • •	• • • •	• • •	• • • •	• • • •	• • •	• • •	• • •	• • • •	• • •	>
3. BO-4	1kD			880			890				)		-	910
[ 3684 ]	::•	• • • • •	• • • •	• • • • •	• • • •	• • •	• ••	• •••	•••	• • •	• • •	• • • •	- • •	>
4. DK29 [ 3672 ]				880			890 • • •		• • •	90	D • ••			910 >

	5. PKO-41)												900			91	
I	3672 ]	• • •	•••	•••	•••	•••	•••	•••	•••	•••	•••	•••	•••	•••	• • •	•••	•••>
			,	220			030			9,	10			250			060
		*														*	
<b>B</b> .	31-41kD														ATG		
	1. KA-41kI																
i	3996 ]												•••	•••	• • •	•••	>
ſ	2. P-Gau-4													950			960
																•••	
	3. BO-41kI 3684 }																960 • • • >
ſ	4. DK29-4: 3672 ]	1	:	920			930	. at		94	10		:	950			960
	5. PKO-411 3672 ]																960 >
				9	70			980			990		_	10	00		
B.	31-41kD	ATT	GCG	CAG	GCT	AAT	CAA	GTT	CCC	CAA	TAT	GTT	TTG	TCA	TTG	CTT	AGA
		TAA	CGC	GTC	CGA	TTA	GTT	CAA	GGG	GTT	ATA	CAA	AAC	AGT	AAC	GAA	TCT
т	1. KA-41ki 3996 ]													100			
•	•															•••	>
ſ	2. P-Gau-4	4	a	9	70			980	t		990			100	00		
•	3. BO-41ki															•••	••••
ſ	3684 ]													100			>
	4. DK29-4	1		9'	70			980			990			10	00		
I	3672 ]	• • •	•••	a	•••	• • •	• • •	• • •	t	•••	•••	• • •	• • •	•••	• • • •	• • •	ج>
_	5. PKO-41							980						10	00		
I	3672 ]	•••	a	•••	•••	•••	•••	• • •	t	•••	• • •	• • •	• • •	• : •	• • •	• • •	>
	10	010															
В	31-41kD	TAA ATT															
I	2. P-Gaul	010	>														

Sequence Rar	nge: 1 to 822	•	
	10	20 30	40
OspA-B31	ATG AAA AAA TAT TTA TTG TAC TTT TTT ATA AAT AAC	GGA ATA GGT CTA CCT TAT CCA GAT	ATA TTA GCC TTA ATA GCA TAT AAT CGG AAT TAT CGT
OspA-B31 [ 3288 ]		20 30	40
Ospa-KA [ 3288 ]		20 30	
Ospa-N40 [ 3276 ]		20 30	40
OspA-2S7 [ 3264 ]	10	20 30	40
OspA-25015 [ 2802 ]	10	20 30	t>
OSPA-TRO [ 2648 ]		20 30	40
OspA-K48 [ 2584 ]	10	20 30	>
OspA-HE 11 [ 2580 ]	10	20 30	>
OspA-DK29 [ 2566 ]	10	20 30	
OspA-1p90 [ 2562 ]	10	20 30	40 a>
OspA-BO [ 2558 ]	. 10.	20 30	40
OSPA-IP3 [ 2558 ]	10	20 30	>
OspA-PKO [ 2558 ]	10	20 30	40
Ospa-ACAI [ 2556 ]		20 30	40
ospa-P-GAU [ 2544 ]		20 30	40
	50 60	70	80 90
OspA-B31	TGT AAG CAA AAT GTT AG ACA TTC GTT TTA CAA TC	C AGC CTT GAC GAG G TCG GAA CTG CTC	AAA AAC AGC GTT TCA GTA TTT TTG TCG CAA AGT CAT

FIGURE 42 (1 of 16)

111	//33
"	//30

OspA-B31	50	60	70	80	90
[.3288] Ospa-KA	50	60	70	80	90
[ 3288 ]	•••			80	90
OspA-N40 [ 3276 ]	50	60	70		>
OspA-ZS7 [ 3264 ]	50	60	70	80	90 >
OspA-25015 [ 2802 ]	50	60	70 	80	90 >
OspA-TRO [ 2648 ]	50	60	70 t	80	90>
OspA-K48 [ 2584 ]	50	60	70t	80 at	90
OspA-HE 11 [ 2580 ]	50	60	70 t	80 .at	90>
OspA-DK29 [ 2566 ]	50	60	70t	80 .at	90>
OspA-Ip90 [ 2562 ]	50	60	70 t	80 .at	90>
OspA-BO [ 2558 ]	50	60	70t	80 .a	90 .c>
OSPA-IP3 [ 2558 ]	50	60	70t	80 .a	90 .c>
OspA-PKO [ 2558 ]	50	60	70t	80 .a	90 .c>
Ospa-ACAI [ 2556 ]	50 c	60	70t	80 .a	90 .c>
ospa-P-GAU [ 2544 ]	50c	60	70t	80 .a	90 .c>
	100	110	120	130	140
OspA-B31	GAT TTG CCT CTA AAC GGA	GGT GAA ATG	AAA GTT CTT G	TA AGC AAA GAA AT TCG TTT CTT	AAA AAC AAA TTT TTT TTT
OspA-B31 [ 3288 ]	100	110	120	130	140>
OspA-KA [ 3288 ]	100	110	120	130	140>
Ospa-N40	100	110	120	130	140

FIGURE 42 (2 of 16)

		•			
[ 3276 ]	!	••• •••	c ····	•••	>
Ospa-257 [ 3264 ]	100		120 c		140>
OspA-25015 [ 2802 ]	100			130	140 g>
OspA-TRO [ 2648 ]	100 a	110	120	130	140 g>
OspA-K48 [ 2584 ]	100 a	110 g	.c	t	140 g>
OspA-HE 11 [ 2580 ]	100 a	110 g	120	<del>1</del> 30 t	140 g>
OspA-DK29 [ 2566 ]	100 a	110 g	.c	130 t	140 g>
OspA-Ip90 [ 2562 ]	100 a	110 g	120 c	130 t	140 g>
OspA-BO [ 2558 ]	100	110 g		130	140 g>
OSPA-IP3 [ 2558 ]	100	110 gt	120	130	140 g>
OspA-PKO [ 2558 ]	100	110 g	120	130 t	140 g>
Ospa-ACAI [ 2556 ]	100	110 g	120 '	130	140 g>
ospA-P-GAU [ 2544 ]	. 100	110 g	120	130 t	140 g>
	150	160	170	180	190
OspA-B31	GAC GGC AAG CTG CCG TTC	TAC GAT CTA ATG CTA GAT	ATT GCA ACA GTA TAA CGT TGT CAT	GAC AAG CTT CTG TTC GAA	GAG CTT AAA CTC GAA TTT
OspA-B31 [ 3288 ]	150	160	170	180	190
Ospa-Ka [ 3288 ]	150	160	170	180	190
OspA-N40 [ 3276 ]	150	160	170	180	190
OspA-ZS7 [ 3264 ]	150	160	170	180	190>
OspA-25015 [ 2802 ]	150	160 ag	170	180	190

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OspA-TRO [ 2648 ]	150 tt .	.a	160 ag	g .	170	· • • • •	180 a	•••	190>
OspA-X48 [ 2584 ]	150 t.	.a	160 ag	gag .	170		180	•••	190
OspA-HE 11 [ 2580 ]	150 tt .	.a	160 ag	g .	170	a	180	•••	190>
OspA-DK29 [ 2566 ]	150 t .	.a	160 ag	gag .		. :	180	•••	190>
OspA-Ip90 [ 2562 ]	150 tt .	.a	160 ag	g .	170		180	•••	190>
OspA-BO [ 2558 ]	150 t .		160 ag	.ag .	170		180 a	•••	190 a>
OSPA-IP3 [ 2558 ]	150 t .		160 ag	.ag .	170		180 a	• • • ·	190 a>
OspA-PKO · · [ 2558 ]	150t .		160 ag	.ag .	170	• • • •	180 a	•••	190 a>
Ospa-ACAI [ 2556 ]	150 t .		160 ag	.ag .	170		180 a		190 a>
	3.50		160		170		180		190
ospa-P-GAU [ 2544 ]	150 t .			.ag .	• • • • • •	• • • •	a	•••	a>
	t .	00					230	•••	
	t .	DO TOT GAT	210 * * AAA AAC	AAT (	220	• GA GTA	230 CTT GAA	GGC	240 GTA AAA
[ 2544 ]	GGA ACT T	DO TOT GAT	210 * * AAA AAC	AAT (	220	ea GTA CAT	230 CTT GAA GAA CTT 230	GGC	240 GTA AAA
[ 2544 ] OspA-B31 OspA-B31	GGA ACT T	DO TCT GAT AGA CTA	ag 210 * AAA AAC TIT TIG	AAT (	220 GGA TCT GC CCT AGA CC	CA GTA	230 CTT GAA GAA CTT		240 GTA AAA CAT TIT
[ 2544 ] OspA-B31 [ 3288 ] OspA-KA	GGA ACT TCCT TGA A	DO TCT GAT AGA CTA	210 210 AAA AAC TTT TTG 210	AAT (	220 220 220	CA GTA	230 CTT GAA GAA CTT 230	 ecc ccc	240 GTA AAA CAT TIT 240 >
OspA-B31 OspA-B31 [ 3288 ] OspA-KA [ 3288 ] OspA-N40	GGA ACT TCCT TGA #	TCT GAT AGA CTA	210 * AAA AAC TTT TTG 210 210	AAT (	220 GGA TCT GC CCT AGA CC 220 220	EA GTA ET CAT	230 CTT GAA GAA CTT 230 230	 ecc cce	240 GTA AAA CAT TIT 240 240 240
OspA-B31 OspA-B31 [ 3288 ] OspA-KA [ 3288 ] OspA-N40 [ 3276 ] OspA-Z57	20 GGA ACT T CCT TGA #	TCT GAT AGA CTA  00  00  00  00  00	210 AAA AAC TIT TIG 210 210 210	AAT (TTA (	220 220 220 220 220	DA GTA	230 CTT GAA GAA CTT 230230	 	240 GTA AAA CAT TIT 240 240 240 240 240
OSPA-B31   OSPA-B31   3288   OSPA-KA   3288   OSPA-N40   3276   OSPA-Z57   3264   OSPA-25015	20 GGA ACT TCCT TGA 3	TCT GAT AGA CTA  00  00  00  00  00	210 AAA AAC TIT TIG 210 210 210 210 210 210	AAT (TTA (	220 220 220 220 220	DA GTA	230 CTT GAA GAA CTT  230 230 230 230 230 230		240 GTA AAA CAT TIT  240 240 240 240 240 240 240

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			220 240
OSPA-HE 11 [ 2580 ]	200 210c	220 .t ac	230 240t .a>
OspA-DK29 [ 2566 ]	200 210	220 .t ac	230 240t .a>
OspA-Ip90 [ 2562 ]	200 210c .	220 .t ac	230 240
OspA-B0 [ 2558 ]	200 210 g	220 .tgg	230 240 t ac>
OSPA-IP3 [ 2558 ]	200 210 g	220 .tg	230 240 t ac>
OspA-PKO [ 2558 ]	200 210 g	220 .tgg	230 240>
Ospa-ACAI [ 2556 ]	200 210	220 .tg	230 240 t ac>
ospa-P-GAU [ 2544 ]	200 210	220	230 240
• === •	250 260	270	280
OspA-B31	GCT GAC AAA AGT AAA GTA AAA T CGA CTG TTT TCA TTT CAT TTT A	TA ACA ATT TCT GA	C GAT CTA GGT CAA G CTA GAT CCA GTT
OspA-B31 [ 3288 ]	250 260	270	280
OspA-KA [ 3288 ]	250 260	270	280
OspA-N40 [ 3276 ]	250 260	270	280 >
OspA-ZS7 [ 3264 ]	250 260	270 	280>
OspA-25015 [· 2802 ]	250 260	270 g	280 a.c ac.>
OspA-TRO [ 2648 ]	250 260 tc	270	280 .a a a>
OspA-K48 [ 2584 ]	250 260 a	270 g	280 .tc a>
OspA-HE 11 [ 2580 ]	250 260 a	270 g	280 .g a a>
OspA-DK29 [ 2566 ]	250 260 a	270 .c g	280 .tc a>
OspA-Ip90	250 260	. 270	280

FIGURE 42 (5 of 16)

	- /
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[ 2562 ]	a	•••	• • •	•••	•••	.c.	• • •	•••	•••	•••	g	g	•••	•••	a	a>
OspA-BO [ 2558 ]	.a.	٠	25	50			260	•••		270		• • •			•••	a>
OSPA-IP3 [ 2558 ]	.a.		25	50	•••		260		•••			. • • •			a	a>
OspA-PKO [ 2558 ]	.a.			50			260	•••		270 				BO •••	• • •	a>
Ospa-ACAI [ 2556 ]	.a.			50			260		•••			•••		30	a	a'>
ospa-P-GAU [ 2544 ]	.a.	•••		50	•••		260		•••	270.		• • •		30	a	a> ·
	290			300			3:	10	•	į	320		*	330		
OspA-B31	ACC TGG	ACA TGT	CTT GAA	GAA	GTT	TTC	AAA	GAA	GAT	GGC	AAA	ACA	CTA	GTA	TCA	AAA TTT
OspA-B31 [ 3288 ]	290			300		•••					320	•••		330		>
Ospa-Ka [ 3288 ]	290			300					•••		320		•••	330		>
OspA-N40 [ 3276 ]	290			300				10			320		•••	330	•••	>
OspA-ZS7 [ 3264 ]	290		· • • •									• • •		330		>
OspA-25015 [ 2802 ]	290			300		a					320		t	330 g		>
OspA-TRO [ 2648 ]	290		t	300							320		t	330		>
OspA-K48 [ 2584 ]	290 t		t	300				10			320		t	330		>
OspA-HE 11 [ 2580 ]	290		t	300	a.c	•••					320	• • •	t	330	g	>
OspA-DK29 [ 2566 ]		.a.	t	300		•••					320		t	330		>
OspA-Ip90 [ 2562 ]					a.c						320	• • •	t	330		>
OspA-BO [ 2558 ]	290		t.c	300				10			320	• • •	t	330 g		.g.>
OSPA-IP3 [ 2558 ]	290		t.c	300				10	•••		320	• • •	t	330 g	•••	.g.>

FIGURE 42 (6 of 16)

OspA-PKO [ 2558 ]	290 t.c	300 c	310	320	330 tgg.>
Ospa-ACAI [ 2556 ]	290 t.c	300 c	310	320	330 tgg.>
ospA-P-GAU [ 2544 ]	290 t.c	300 c	310 a ···	320	330 tgg.>
	340	350	360	· 370	380
OspA-B31	AAA GTA ACI TTT CAT TGA	TCC AAA GA AGG TTT CT	C AAG TCA TO G TTC AGT AO	A ACA GAA GAA T TGT CTT-CTT	AAA TIC AAT GAA TIT AAG TIA CIT
OspA-B31 [ 3288 ]	340	350	360	370	380
OspA-KA [ 3288 ]	340	350	360	370	380>
Ospa-N40 [ 3276 ]	340	350	360	370	380>
OspA-ZS7 [ 3264 ]	340	350	360	370	380>
OspA-25015	340 ag	350 t	360 t	370	g>
OspA-TRO [ 2648 ]	340 a	350 t	360 .t	370 t	380 c .c.>
OspA-K48 [ 2584 ]	340	350 c ctt	360	370	380c>
OspA-HE 11 [ 2580 ]	340	350 c ctt	360	370	380 c>
Ospa-DK29 [ 2566 ]	340	350 c ctt	360	370	380 c .g.>
OspA-Ip90 [ 2562 ]	340	350 c ctt	360	370	380 c .c.>
OspA-BO [ 2558 ]	3409	350	360 a a	370 t	380>
OSPA-IP3 [ 2558 ]	340 9	350 t	360 a a	370 t	380>
OspA-PKO [ 2558 ]	340	350 Jt	360 aa	370 t	.tg>
OspA-ACAI [ 2556 ]	340	350 gt	360 a a	370 t	380 . .tg>

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ospa-P-GAU [ 2544 ]		350 gt .g.	0 ga	360 a	370 t	.tg>
	390	•	400	410	420	430
OspA-B31	ANA CCT	CAR CTA TY	CT GAA AAA	ATA ATA AC	A AGA GCA	GAC GGA ACC AGA CTG CCT TGG TCT
OspA-B31 [ 3288 ]	390	••• •••	400	410	420	430
OspA-KĀ [ 3288 ]	390	••• •••	400	410	420	430
OspA-N40 [ 3276 ]	• • • • • •				• • • • • • •	430>
OspA-ZS7 [ 3264 ]	390	••• •••	400	410	420	430
OspA-25015 [ 2802 ]	390 c	t g	400 t	410 g g.	420	430 at.>
OspA-TRO [ 2648 ]	390	t	400	410 .c ct	420	430 ag>
OspA-K48 [ 2584 ]	390	ac	400	410 .c gt	420	430 a.t>
OspA-HE 11 [ 2580 ]	390 g	a	400	410 .c gt	420	430 a.t>
OspA-DK29 [ 2566 ]	390 g	ac	400	410 .c gt	420	430 a.t>
OspA-Ip90 [ 2562 ]	390 g	c	400	410 .c gt	420	430 a.t>
OspA-BO [ 2558 ]	390	t.g .	400 c	410 .ccg	420 a.	430 a.ta.>
OSPA-IP3 [ 2558 ]	390	t.g .	400 c	410 .ccg	420 a.	430 a.ta.>
OspA-PKO [ 2558 ]	390	t.g .	400 c	410 .ccg		430 a.ta.>
Ospa-ACAI [ 2556 ]	390	t.g .	400 c	410 .ccg	420 a.	430 a.ta.>
ospA-P-GAU [ 2544 ]	390	t.g .	400 c	410 ccg	420 a.	430 a.t ,a.>
	4	140	450	460	•	470 480
OspA-B31	CTT GAA	TAC ACA C	GGA ATT AAJ	A AGC GAT GO	A TOT GGA	AAA GCT AAA GAG

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	GAA CTT ATG TGT CCT TAA TT	TCG CTA CCT AGA	CCT TTT CGA TTT CTC
OspA-B31 [ 3288 ]		460	470 480>
OspA-KA [ 3288 ]	440 450	460	470 480>
OspA-N40 [ 3276 ]	440 450a	460	
OspA-ZS7 [ 3264 ]	· 440 450	460	470 480
OspA-25015 [ 2802 ]	440 450	460	470 480a>
Ospa-TRO [ 2648 ]	440 450 aa	460 a.c	470 480
OspA-K48 [ 2584 ]	440 450 aca		470 480a>
OspA-HE 11 [ 2580 ]	440 450 aca	460 aa. a.c	470 480a>
OspA-DK29 [ 2566 ] ·	440 450aca		470 480 
OspA-Ip90 [ 2562 ]	440 450aca		470 480a>
OspA-BO [ 2558 ]	440 450 tag	460 a.c	
OSPA-IP3 [ 2558 ]	440 450 tag	460 a.c	470 480 a>
OspA-PKO [ 2558 ]		460 a.c	470 480a>
OspA-ACAI [ 2556 ]	440 450 tag	460 a.c	470 480a>
ospA-P-GAU [ 2544 ]		460 a.c	470 · 480 ·
	490 500	510	520
OspA-B31	GTT TTA AAA GGC TAT GTT CT CAA AAT TTT CCG ATA CAA GA	T GAA GGA ACT CTA A CTT CCT TGA GAT	ACT GCT GAA AAA ACA TGA CGA CTT TTT TGT
OspA-B31 [ 3288 ]	490 500	510	520>
OspA-KA [ 3288 ]	490 500		520

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Ospa-N40 [ 3276 ]	•••	490	500	510	520	••••
OspA-ZS7 [ 3264 ]		490 . a	500	510 t	520	
OspA-25015 [ 2802 ]		<b>4</b> 90 aa	500	510	520	g>
OspA-TRO [ 2648 ]		490 at.	.c	510	520 gcc	
	•				cgg	
OspA-K48 [ 2584 ]		490 at.	500 ac	510	5201 gc	530
					cgg	
OspA-HE 11 [ 2580 ]	*** ****	490 at.	500 ac	510	5201 gc	530>
					cgg	
OspA-DK29 [ 2566 ]		490 at.	500 ac	510	5201 gc	530
				•	cgg	
OspA-Ip90 [ 2562 ]		490 at.	500 .c	510	5201 gc	530
OspA-BO [ 2558 ]		490 . aat.	500 ac	510 aa g	520 g aat	gt.>
OSPA-IP3 [ 2558 ]		490 . aat.	500 ac	510 aa g	520 g aat	gt.>
OspA-PKO [ 2558 ]		490 . aat.	500 ac	510 aa g	520 g aat	gt.>
OspA-ACAI [ 2556 ]		490 . aat.	500 ac	510 aa g	520 g aat	gt.>
ospa-P-GAU [ 2544 ]		490 . aag .t.	500 ac	510 aa g	520 gaat	gt.>
	530	540	550	560	570	
	* *	•		* *	* *	*
OspA-B31	ACA TTG GT	AC CAA TTT	CTT CCT TGA	GTT ACT TTA CAA TGA AAT	TCG TTT TTA	TAA AGT
OspA-B31	530	540	550	560	570	
[ 3288 ]					••••	>
Ospa-Ka	530	540	550	560	570	

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[ 3288 ]	•••		• • • • • • • • • • • • • • • • • • • •	••• ••• •••	>
OspA-N40 [ 3276 ]	530	540	550	560	570 >
OspA-ZS7 [ 3264 ]	530	540	550	560	570 >
OspA-25015 [ 2802 ]	530	540	550	560	570
Ospa-TRO	530	540	550	560	570 c.c c>
OspA-K48 [ 2584 ]		540	550	560- gt	570
OspA-HE 11 [ 2580 ]		540	550	560	570
OspA-DK29 [ 2566 ]		540	550	560 gt	570
OspA-Ip90		540	550		570
[ 2562 ] OspA-BO	530	540	550	560	570
[ 2558 ] OSPA-IP3	530	540	550	560	g g.a g>
[ 2558 ]				t	
OspA-PKO [ 2558 ]	530	540 .aaa	550 c	560 t	570 g g.a g>
Ospa-ACAI [ 2556 ]	530	540 .aaa	550 c	560t	570 g g.a g>
ospA-P-GAU [ 2544 ]	530	540 .aaa	550 c	560 t	570 g g.a g>
, .	580	590	600	610	620
OspA-B31	AAA TCT TTT AGA	GGG GAA GT	r TCA GTT GAA	CTT AAT GAC ACT GAA TTA CTG TGA	GAC AGT AGT GCT
OspA-B31 [ 3288 ]	580	590		610	620
OspA-KA [ 3288 ]	580	590	600	610	620
OspA-N40 [ 3276 ]	580	590	600	610	620>
OspA-ZS7	580	590	600	610	620

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OspA-25015 [ 2802 ]		a •		60Ô	610	620
OspA-TRO [ 2648 ]	580 c	590 a a		600 g	610 t.	620 . a tcc. cag>
Ospa-K48 5 [ 2584 ]	80 c	590 a a		0 c		620 cc. cag>
OspA-HE 115 [ 2580 ]	80 ċ	590 a a	· 60		610 g	620 tcg>
OspA-DK29 5 [ 2566 ]	80 c	590 · a a.	60 a ac		610 gt.	620 cc. cgg>
OspA-Ip90 5	¢	590 a a.	60 .a a		610 t.	620 cc. cag>
OspA-BO [ 2558 ]	580	590 a		600 ct	610	620 . acc. cag>
OSPA-IP3 [ 2558 ]	580	590 a			610	620 . acc. cag>
OspA-PKO [ 2558 ]	580	590 a			610	620 . acc. cag>
OspA-ACAI [ 2556 ]	580	590 a	) .a a	600 ct	610	620 . acc. cag>
ospA-P-GAU [ 2544 ]	580	590		600 ct	610	620 . acc. cag>
	630	*	640	650	* 1	•
OspA-B31	GCT ACT CGA TGA	OX AAA AAA OT TTT TTT	T GCA GCT	TGG AAT ACC TTA	TCA GGC ACT	TOA ACT TTA ACA AGT TGA AAT TGT
OspA-B31 [ 3288 ]	630		640	650	660	670
OspA-KA [ 3288 ]	630		640	650	66	670
OspA-N40 [ 3276 ]	630	•••	640	650	660	• • • • • • • • • • • • • • • • • • • •
OspA-ZS7 [ 3264 ]	630	•••	640	650	660	670
OspA-25015 [ 2802 ]	630		640 gg aaa	650 g	g	670
OspA-TRO [ 2648 ]	630			650	660 aat	670

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OspA-K48 [ 2584 ]	630	640 g.	650 aaa g	660 aaa	670 c >
OspA-HE 11 [ 2580 ]	630 a	640 t.c .g.	650 a.a g		670 t>
OspA-DX29 [ 2566 ]	630	640 g.	650 aaa g	660 . aag	670 c>
OspA-Ip90 [ 2562 ]	630	640 g.	650 a.a g	660 . aag	670 c>
OspA-BO [ 2558 ]	630	640 gc	650 a g		670
OSPA-IP3 [ 2558 ]	630	640 gc	650 a g	660 . aaa	670
OspA-PKO [ 2558 ]	630	640 gc	650 a g	660 . aaat	670
Ospa-ACAI [ 2556 ]	630	640 gc	650 a g	660 . aaat	670
ospA-P-GAU [ 2544 ]	630	640 gc	650	660 . aaat	670
	680	690	700	710	720
OspA-B31	ATT ACT GTA TAA TGA CAT	AAC AGT AAA TIG TCA TIT	AAA ACT AAA GA TTT TGA TTT CT	CTT GTG TTT GAA CAC AAA	ממם מממ בחמי
OspA-B31 [ 3288 ]	680	690	700	710	720
OspA-KA [ 3288 ]	680	690	700	710	720 >
Ospa-N40 [ 3276 ]	680	690	700	710	720 ··· ···>
OspA-ZS7 [ 3264 ]	680	690	700	710	720
OspA-25015 [ 2802 ]	680	690 ac	700c.	710 a	720 c>
OspA-TRO [ 2648 ]	680 gg	690 tc	700 a	710 aa	720 >
OspA-K48 [ 2584 ]	680 gg	690 tc c	700 a	710 ac	720 >
OspA-HE 11 [ 2580 ]	680 g. aa.	690 a c	700	710	720 >
OspA-DK29	680	690	700	710	720

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[ 2566 ] .	ggtc cc aac
OspA-Ip90 [ 2562 ]	680 690 700 710 720ggtc cgc aac
OspA-BO [ 2558 ]	680 690 700 710 720gtc .c. c.at c>
OSPA-IP3 [ 2558 ]	680 690 700 710 720gtc. c.a
OspA-PKO [ 2558 ]	680 690 700 710 720gtc. c.a
OspA-ACAI [ 2556 ]	680 690 700 710 720gtcc. c.a
ospA-P-GAU [ 2544 ]	680 690 700 710 720gtcc. c.a
	730 740 750 760
OspA-B31	AAC ACA ATT ACA GTA CAA CAA TAC GAC TCA AAT GGC ACC AAA TTA GAG TTG TGT TAA TGT CAT GTT GTT ATG CTG AGT TTA CCG TGG TTT AAT CTC
OspA-B31 [ 3288 ]	730 740 750 760
OspA-KA [ 3288 ]	730 740 750 760
Ospa-N40 [ 3276 ]	730 740 750 760
OspA-ZS7 [ 3264 ]	730 740 750 760
OspA-25015 [ 2802 ]	730 740 750 760 g tc a gcaacga>
OspA-TRO [ 2648 ]	730 740 750 760 gaagcatca>
OspA-K48 [ 2584 ]	730 740 750 760 770 g
OspA-HE 11 [ 2580 ]	730 740 750 760 g a a.c
OspA-DK29 [ 2566 ]	730 740 750 760 770 gaag gcat cay
OspA-Ip90 [ 2562 ]	730 740 750 760 770 g a
OspA-BO [ 2558 ]	730 740 750 760 g a

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		360
OSPA-IP3 [ 2558 ·]	730 740 750 gatac.gcat	760 ta>
OspA-PKO [ 2558 ]	730 740 750 gata	760 t a>
OspA-ACAI [ 2556 ]	730 740 750 gata	760 ta>
ospa-P-GAU [ 2544,]	730 740 750 t at a gcat	760 t <sub>.</sub> a>
	770 780 790 800	810
OspA-B31	GGG TCA GCA GTT GAA ATT ACA AAA CTT GAT GAA ATT CCC AGT CGT CAA CTT TAA TGT TTT GAA CTA CTT TAA	AAA AAC GCT TTA TTT TTG CGA AAT
OspA-B31 [ 3288 ]	770 780 790 800	810
OspA-KA [ 3288 ]	770 780 790 800	810
OspA-N40 [ 3276 ]	770 780 790 800	810
OspA-ZS7 [ 3264 ]	770 780 790 800	810 >
OspA-25015 [ 2802 ]	700 800	810
Ospa-TRO [ 2648 ]	770 780 790 800c aac	810
OspA-K48 [ 2584 ]		810
OspA-HE 11 [ 2580 ]	700 800	810
OspA-DK29 [ 2566 ]	200 800	810
OspA-Ip90 [ 2562 ]	780 790 800	810
OspA-BO [ 2558 ]	770 780 790 800c a c ac c.	810
OSPA-IP3 [ 2558 ]	770 780 790 800c a c ac c.	810
OspA-PKO [ 2558 ]	770 780 790 800c a c.	810

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OspA-ACAI 770 [ 2556 ]c	780 ac		c	810 ·····g>
ospa-P-GAU 770	780	790	800	810
[ 2544 ]c	ac	ac	c	
82	0			
Ospa-B31 AAA 1				
OspA-B31 82 [ 3288 ]				
OspA-KA 82				
OspA-N40 82				
OspA-ZS7 826 3264 ]				
OspA-25015 [ 2802 ] .g.>	•			
OspA-TRO 82				
OspA-K48 820 [ 2584 ]				
OspA-HE 11 82 [ 2580 ]				
OspA-DK29 820 [ 2566 ]	>			
OspA-Ip90 820 [ 2562 ]	>			
OspA-BO 82 ( 2558 )				
OSPA-IP3 82 [ 2558 ]				
OspA-PKO 82 [ 2558 ]				
OspA-ACAI 82 [ 2556 ]	0			
ospa-P-GAU 82	0			

FIGURE 42 (16 of 16)

	10	20	30	•	40
ATG AAA AAA TAC TTT TTT	ATT TAT TAA ATA	TTG OGA ATA AAC CCT TAT	GGT CTA CCA GAT	ATA TTA (	GCC TTA ATA
50	60	*	70	80	90
GCA TGT AAG CGT ACA TTC	CAA AAT GTT TTA	GTT AGC AGC CAA TCG TCC	CTT GAT	GAA AAA A	AAT AGC GTT ITA TCG CAA
. 10	00	110	120		130
TCA GTA GAT AGT CAT CTA	TTA CCT AAT GGA	GGT GGA ATO CCA CCT TAO	ACA GTT TGT CAA	CTT GTA	AGT AAA GAA TCA TIT CTT
140	150	± 1	.60	170	180
AAA GAC AAA TTT CTG TTT					
19	90	200	210	•	220
CTT GAG CTT GAA CTC GAA	AAA GGA TTT CCT	ACT TCT GAT	AAA AAC	AAC GGT TTG CCA	TCT GGA ACA AGA CCT TGT
230	240	. 2	250	260	270
CTT GAA GGT GAA CTT CCA	GAA AAA CIT TTT	ACT GAC AAI	AGT AAA TCA TTT	GTA AAA (	TTA ACA ATT AAT TGT TAA
. 2	80	290	300	•	310
GCT GAT GAC CGA CTA CTG					
320	330	•	340	350	360
OCC AAA ACA					
, 3	70	380	390	•	400
TCA ACA GAA AGT TGT CTT					TCT GAA AAA AGA CTT TTT
410	420	<b>*</b>	430	440	450
	AGA GCA	AAT GGA AC	AGA CTT	GAA TAC	ACA GAC ATA TGT CTG TAT
<b>4</b>	60	470	480	•	490
AAA AGC GAT TTT TCG CTA	GGA TCC	GGA AAA GC CCT TTT CG	r aaa gaa a tii cii	GTT TTA	AAA GAC TTT TTT CTG AAA
500	510	*	520	530	540
ACT CTT GAA TGA GAA CTT	GGA ACT	CTA GCT GC GAT CGA CG	T GAC GGC A CTG CCG	AAA ACA	ACA TTG AAA TGT AAC TTT
• 5	550	560	570		580

K48/Tro Ospa Wednesday, April 27, 1994 11:37 AM CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA AAT TTT AGG 630 590 GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT CAG GCT CCT CTT TAT TGT CAA CGT GAA CTA CTG AGA CTG TGA TGA GTC CGA 650 670 660 640 \* \* ŧ ACT ANA ANA ACT OGA ANA TOG GAT TOA ANT ACT TOO ACT TTA ACA TGA TIT TIT TGA CCT TIT ACC CTA AGT TTA TGA AGG TGA AAT TGT 690 700 ATT AGT GTG AAT AGC AAA AAA ACT AAA AAC ATT GTA TIT ACA AAA TAM TOA CAC TIM TOG TIT TIT TGA TIT TIG TAM CAT AMA TGT TIT 750 730 GAA GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTT CTG TGT TAT TGT CAT GIT TTT ATG CTG AGT CGT CCG TGG TTA 790 800 810 770 780 CTA GAA GGC AAC GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA GAT CTT CCG TTG CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT

AAC GCT TTA AAA TAG TTG CGA AAT TTT ATC

Figure 43 (2 of 2)

	•	. 1	R	*		20		•	30		•		<b>10</b>	•
ATG A	AA! TT	AAA TTT	TAT ATA	ATT TAA	TTG AAC	GGA CCT	ATA TAT	GCT CCA	CTA GAT	ATA TAT	att Aat	CCC	ATT TAA	ata Tat
•	50			60		•	•	70 *	•		80		•	90
GCA C	TGC ACG	AAG TTC	CAA GTT	TAA ATT	GTT CAA	AGC TCG	AGC	CTT GAA	GAT CTA	GAA	AAA TTT	AAC TTG	AGC TCG	GCT CGA
		1	00	•		110		•	120	ء ۔	= ::- •	. 1	30	•
TCA AGT	GTA CAT	GAT CTA	TTG	CCT GGA	CCA	CAG	TAC	AAA TTT	CAA	GAA	CAT	agt TCA	AAA TTT	GAA CTT
1	40			150		•	1	.60		1	170		*	180
AAA TTT	GAC CTG	AAA TTT	GAC	CCA	DAA	TAC	AGA TC	CTA A GAI	AAC	CGT	ACA TGI	CAT CAT	GAC	AAG TTC
		1	.90			200		*	210	<b>)</b>	•	2	20	•
ATT TAA	GAG CTC	CTA GAT	AA A	GGA CCT	LOA L	TCT A AGA	r ga a ct	AAZ A TT	GAC CTY	AA' TT	r GG1 A CC2	TC:	r GGA CCT	GTG
	230			240	k .	4		250		•	260		•	270
CTT GAA	GAA	, cc	I ACI	AA AAI	A GA	r ga a cr	C AA G TT	a ag T TC	T AA TT	A GC T CG	A AAI T TT	TT A	A ACA	ATT TAA
			280		<b>4</b>	290 *			30	•			310	•
GCT CGA	GA(	GA G CT	T CT A GA	A AG T TC	T AA TT	A AC T TG	C AC	TT AS	4.D 24	A CT	TT TY	AA A TT T	A GAI T CT	A GAT I CTA
	320		_	33	0			340			350		•	360
CCC	AA : TT :	A AC	A TI	A GT	G TC	A AC	A A	AA G1	A AT	OT TO	OA TO	A GA	C AA	A ACA T TGT
			370		*	380	0	*	3	90			400	*
TC! AG	AC OT T	A GA	AT GA	A AZ	NG TY	IC AI AG T	AT G TA C	AA AA T TT	AA G	GT G CA C	AA T	IG TO	CT GC GA CG	AAA A TIT T
	410			42	20		*	430 *		*	44		•	450
AC TG	ר אי	V: 30	CA A	GA G	AA A	AT G TA C	GA A	CC A	AA C	TT C	T AA A TT	A TA T AT	CA GI GT C	A ATG
			450			47	0	•	. 4	180		•	490 *	•
AA TT	A A T T	3C G	AT G	GA A	œ 0	GA A	AA (	CT A	AA (	AAE TTC	TT T	A AT I TA	AA A	ag tit TC aaa
	50	0		. 5	10		•	520	•	•	53	0	*	540 *
). OT	T C	TT C	AA: O TT	GA A	AA (	CAT (	GCT CGA	AAT (	CTA	AAA TTT	CAT 1	CA 1	MTG G	AA GTA TT CAT
			550	h	•		60		ŧ	570		•	580	*
A.	AA G	ÄA (	GGA A	ACC (	TT.	ACT '	TTA	ACT	AAG	GAA	TTA	GCA .	AAA 1	nct oga

P-GAU/BO-OSPA Wednesday, April 27, 1994 11:22 AM

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TTT CTT CCT TGG CAA TGA AAT TCA TTC CTT TAA CGT TTT AGA CCT

590 600 610 620 630

GAA GTA ACA GTT GCT CTT AAT GAC ACT AAC ACT ACT CAG GCT ACT
CTT CAT TGT CAA CGA GAA TTA CTG TGA TTG TGA TGA GTC CGA TGA

AGT GTT AAC ACC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA CAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT GTT

GAC ACA ATA ACT GTA CAA AAA TAC GAC TCC GCA GGT ACC AAT TTA CTG TGT TAT TGA CAT GTT TTT ATG CTG AGG CGT CCA TGG TTA AAT

770 780 790 800 810

GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC
CTT CCG TGT CGT CAG CTT TAA TIT TGT GAA CTA CTT GAA TTT TTG

820

GCT TTA AAA TAG CGA AAT TTT ATC

. 10	20	30	40
ATG AAA AAA TAT :	TTA TTG GGA A	TA GGT CTA AT	TA TTA GCC TTA ATA TAT CGG AAT TAT
50	60	70	80 90
GCA TGT AAG CAA A	AAT GTT AGC A TTA CAA TCG T	GC CIT GAC GA GC GAA CTG CT	AG AAA AAC AGC GTT
100	110	120 -	· 130
TCA GTA GAT TTG	CCT GGT GAA A	TG AAA GTT CT	TT GTA AGC AAA GAA
	GGA CCA CIT 1 150	AC TTP CAA GE	LA CAT TCG TTT CTT
•	* *	* *	A ACA GTA GAC AAG
TIT TIG TIT CIG	CCG TTC ATG C	TA GAT TAA CO	T TGT CAT CTG TTC
190	200	210 * *	220
GAA CTC GAA TTT (	GGA ACT TCT G CCT TGA AGA C	AT AAA AAC AF TA TTT TTG TT	AT GGA TCT GGA GTA FA CCT AGA CCT CAT
230	240	250	260 270
CTT GAA GGC GTA I	AAA GCT GAC A TTT CGA CTG T	AA AGT AAA GI TT TCA TIT CI	TTA ACA ATT AAA AT AAT TOT TAA TTT TA
280	290	300	310
TCT GAC GAT CTA ( AGA CTG CTA GAT (	GGT CAA ACC A CCA GTT TGG T	ACA CTT GAA GT	TT TTC AAA GAA GAT AA AAG TTT CTT CTA
320 :	330	340	350 360
GGC AAA ACA CTA	GTA TCA AAA A	AA GTA ACT TO	CC AAA GAC AAG TCA GG TTT CTG TTC AGT
370	380	390	400
TCA ACA GAA GAA	AAA TTC AAT C	BAA AAA GOT GI	AA GTA TCT GAA AAA
			TT CAT AGA CIT TIT
	420	430	440 450
TAT TAT TGT TCT	CGT TTA CCT 1	NGG TIT GAA C	AA TAT ACA GAA ATG
460 * *	470 * *	480	490
AAA AGC GAT GGA . TTT TCG CTA CCT	ACC GGA AAA C	CT AAA GAA G CGA TTT CTT C	TT TTA AAA AAG TTT AAA AAT TTT TTC AAA
500	510	520	530 540
ACT CTT GAA GGA . TGA GAA CTT CCT	AAA GTA GCT A	AAT GAT AAA G FTA ÇTA TTT C	TA ACA TTG GAA GTA AT TGT AAC CTT CAT
550	560	570	580
AAA GAA GGA ACC	GTT ACT TTA	agt aag gaa a	TT TCA AAA TCT GGG

B31-PBK | Hednesday, April 27, 1994 | 11:19 AM

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA AGT TIT AGA COC

590 600 610 620 630

GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT GCT ACT
CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA

640 650 660 670

680 690 700 710 720
AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA

TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT
730 740 750 760

GAC ACA ATA ACA GTA CAR ARA TAC GAC TCA GCA GGC ACC ART CTA
CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT

770 780 790 800 810
GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC
CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG

820

OCT TTA AAA TAA CGA AAT TTT ATT

30 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT 80 70 60 50 GCA TGC AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT CGT ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA 110 TCA GTA GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AGT CAT CTA AAC GGA CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT 160 \* AAA GAC AAA GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG TIT CTG TTT CTG CCA TTC ATG TCA GAT TTC CGT TGT CAT CTG TTC 200 190 ATT GAG CTA AAA GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG TAA CTC GAT TIT CCT TGA AGA CTA TIT CTG TTA CCA AGA CCT CAC 260 240 \* CTT GAA GGT ACA AAA GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GAA CTT CCA TGT TTT CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA 290 300 GCT GAC GAT CTA AGT AAA ACC ACA TTC GAA CTT TTA AAA GAA GAT CGA CTG CTA GAT TCA TIT TGG TGT AAG CTT GAA AAT TIT CTT CTA 320 GGC AAA ACA TTA GTG TCA AGA AAA GTA AGT TCT AGA GAC AAA ACA CCG TIT TGT AAT CAC AGT TCT TIT CAT TCA AGA TCT CTG TIT TGT 390 380 TCA ACA GAT GAA ATG TTC AAT GAA AAA GGT GAA TTG TCT GCA AAA AGT TGT CTA CTT TAC AAG TTA CTT TTT CCA CTT AAC AGA CGT TTT 430 420 ACC ATG ACA AGA GAA AAT GGA ACC AAA CTT GAA TAT ACA GAA ATG TOG TAC TGT TCT CIT TTA CCT TGG TTT GAA CTT ATA TGT CTT TAC 480 AAA AGC GAT GGA ACC GGA AAA GCT AAA GAA GTT TTA AAA AAG TTT TIT TCG CTA CCT TGG CCT TTT CGA TTT CIT CAA AAT TTT TTC AAA 530 510 520 ACT CTT GAA GGA AAA GTA GCT AAT GAT AAA GTA ACA TTG GAA GTA TGA GAA CIT CCT TIT CAT CGA TTA CTA TIT CAT TGT AAC CIT CAT 56C AAA GAA GGA ACC GTT ACT TTA AGT AAG GAA ATT TCA AAA TCT GGG

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA AGT TIT AGA CCC 600 610 GAA GIT TCA GIT GAA CIT AAT GAC ACT GAC AGT AGT GCT GCT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA 660 . 640 650 AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TIT TIT TGA CGT CGA ACC TTA AGT TIT TGA AGG TGA AAT TGT TAA 700 690 \* \* AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT 750 740 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA OGC ACC AAT CTA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 780 790 800 770 GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG OCT TTA AAA TAA CGA AAT TIT ATT



Intern al Application No
PCT/US 94/12352

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/31 C12N15/62 C07K14/20 A61K39/02 G01N33/50 C07K16/12 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) CO7K C12N A61K G01N IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages 1,6,7,9, X MOLECULAR MICROBIOLOGY, 22,27, vol.6, no.20, 1992 28,30,45 pages 3031 - 3040 ROSA P. A. ET AL. 'Recombination between genes encoding major outer surface proteins A and B of Borrelia burgdorferi' see the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed '&' document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report n 3. 03. 95 24 February 1995 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 Espen, J

Form PCT/ISA/210 (second sheet) (July 1992)

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PCT/US 94/12352

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